



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| (22) International Filing Date: 11 June 1998 (11.06.98) | | (73) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US). | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| (30) Priority Data: | | (72) Inventors; and | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <table border="0"> <tr><td>60/049,547</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,548</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,549</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,550</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/050,566</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,606</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,607</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,608</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,609</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,610</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/049,611</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/050,901</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/052,989</td><td>13 June 1997 (13.06.97)</td><td>US</td></tr> <tr><td>60/051,919</td><td>8 July 1997 (08.07.97)</td><td>US</td></tr> <tr><td>60/055,984</td><td>18 August 1997 (18.08.97)</td><td>US</td></tr> <tr><td>60/058,665</td><td>12 September 1997 (12.09.97)</td><td>US</td></tr> <tr><td>60/058,668</td><td>12 September 1997 (12.09.97)</td><td>US</td></tr> <tr><td>60/058,669</td><td>12 September 1997 (12.09.97)</td><td>US</td></tr> <tr><td>60/058,750</td><td>12 September 1997 (12.09.97)</td><td>US</td></tr> <tr><td>60/058,971</td><td>12 September 1997 (12.09.97)</td><td>US</td></tr> <tr><td>60/058,972</td><td>12 September 1997 (12.09.97)</td><td>US</td></tr> <tr><td>60/058,975</td><td>12 September 1997 (12.09.97)</td><td>US</td></tr> <tr><td>60/060,834</td><td>2 October 1997 (02.10.97)</td><td>US</td></tr> <tr><td>60/060,841</td><td>2 October 1997 (02.10.97)</td><td>US</td></tr> <tr><td>60/060,844</td><td>2 October 1997 (02.10.97)</td><td>US</td></tr> <tr><td>60/060,865</td><td>2 October 1997 (02.10.97)</td><td>US</td></tr> <tr><td>60/061,059</td><td>2 October 1997 (02.10.97)</td><td>US</td></tr> <tr><td>60/061,060</td><td>2 October 1997 (02.10.97)</td><td>US</td></tr> </table> | | 60/049,547 | 13 June 1997 (13.06.97) | US | 60/049,548 | 13 June 1997 (13.06.97) | US | 60/049,549 | 13 June 1997 (13.06.97) | US | 60/049,550 | 13 June 1997 (13.06.97) | US | 60/050,566 | 13 June 1997 (13.06.97) | US | 60/049,606 | 13 June 1997 (13.06.97) | US | 60/049,607 | 13 June 1997 (13.06.97) | US | 60/049,608 | 13 June 1997 (13.06.97) | US | 60/049,609 | 13 June 1997 (13.06.97) | US | 60/049,610 | 13 June 1997 (13.06.97) | US | 60/049,611 | 13 June 1997 (13.06.97) | US | 60/050,901 | 13 June 1997 (13.06.97) | US | 60/052,989 | 13 June 1997 (13.06.97) | US | 60/051,919 | 8 July 1997 (08.07.97) | US | 60/055,984 | 18 August 1997 (18.08.97) | US | 60/058,665 | 12 September 1997 (12.09.97) | US | 60/058,668 | 12 September 1997 (12.09.97) | US | 60/058,669 | 12 September 1997 (12.09.97) | US | 60/058,750 | 12 September 1997 (12.09.97) | US | 60/058,971 | 12 September 1997 (12.09.97) | US | 60/058,972 | 12 September 1997 (12.09.97) | US | 60/058,975 | 12 September 1997 (12.09.97) | US | 60/060,834 | 2 October 1997 (02.10.97) | US | 60/060,841 | 2 October 1997 (02.10.97) | US | 60/060,844 | 2 October 1997 (02.10.97) | US | 60/060,865 | 2 October 1997 (02.10.97) | US | 60/061,059 | 2 October 1997 (02.10.97) | US | 60/061,060 | 2 October 1997 (02.10.97) | US | (75) Inventors/Applicants (for US only): MOORE, Paul, A. [GB/US]; Apartment 104, 1908 Holly Ridge Drive, McLean, VA 22102 (US). SHI, Yanggu [CN/US]; 437 West Side Drive, Gaithersburg, MD 20878 (US). ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). LAFLEUR, David, W. [US/US]; 1615 Q Street, N.W. #807, Washington, DC 20009 (US). OLSEN, Henrik, S. [DK/US]; 182 Kendrick Place #24, Gaithersburg, MD 20878 (US). EBNER, Reinhard [DE/US]; 9906 Shelburne Terrace #316, Gaithersburg, MD 20878 (US). BREWER, Laurie, A. [US/US]; 14920 Mt. Nebo Road, Poolesville, MD 20837 (US). YOUNG, Paul [US/US]; 122 Beckwith Street, Gaithersburg, MD 20878 (US). GREENE, John, M. [US/US]; 872 Diamond Drive, Gaithersburg, MD 20878 (US). FERRIE, Ann, M. [US/US]; 13202 L Astoria Hill Court, Germantown, MD 20874 (US). YU, Guo-Liang [CN/US]; 13524 Straw Bale Lane, Damestown, MD 20878 (US). NI, Jian [CN/US]; 5502 Manorfield Road, Rockville, MD 20853 (US). FENG, Ping [CN/US]; 4 Relda Court, Gaithersburg, MD 20878 (US). | |
| 60/049,547 | 13 June 1997 (13.06.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| 60/051,919 | 8 July 1997 (08.07.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| 60/058,668 | 12 September 1997 (12.09.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| 60/058,975 | 12 September 1997 (12.09.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 60/060,834 | 2 October 1997 (02.10.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 60/060,841 | 2 October 1997 (02.10.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 60/060,844 | 2 October 1997 (02.10.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 60/060,865 | 2 October 1997 (02.10.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 60/061,059 | 2 October 1997 (02.10.97) | US | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| | | (74) Agents: BROOKES, A., Anders et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US). | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | | (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
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| (54) Title: 86 HUMAN SECRETED PROTEINS | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| (57) Abstract | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| The present invention relates to 86 novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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86 Human Secreted Proteins

Field of the Invention

This invention relates to newly identified polynucleotides and the polypeptides encoded by these polynucleotides, uses of such polynucleotides and polypeptides, and
5 their production.

Background of the Invention

Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eucaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or
10 organelle, contains different proteins essential for the function of the organelle. The cell uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum
15 (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or
20 secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

Despite the great progress made in recent years, only a small number of genes encoding human secreted proteins have been identified. These secreted proteins include
30 the commercially valuable human insulin, interferon, Factor VIII, human growth hormone, tissue plasminogen activator, and erythropoietin. Thus, in light of the pervasive role of secreted proteins in human physiology, a need exists for identifying and characterizing novel human secreted proteins and the genes that encode them. This knowledge will allow one to detect, to treat, and to prevent medical disorders by using
35 secreted proteins or the genes that encode them.

Summary of the Invention

The present invention relates to novel polynucleotides and the encoded polypeptides. Moreover, the present invention relates to vectors, host cells, antibodies, and recombinant methods for producing the polypeptides and polynucleotides. Also provided are diagnostic methods for detecting disorders related to the polypeptides, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying binding partners of the polypeptides.

Detailed Description

Definitions

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide.

In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X or the cDNA contained within the clone deposited with the ATCC. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, with or without the signal sequence, the secreted protein coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having the translated amino acid sequence generated from the polynucleotide as broadly defined.

In the present invention, the full length sequence identified as SEQ ID NO:X was often generated by overlapping sequences contained in multiple clones (contig

analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X was deposited with the American Type Culture Collection ("ATCC"). As shown in Table 1, each clone is identified by a cDNA Clone ID (Identifier) and the ATCC Deposit Number. The ATCC is located at 10801 University Boulevard,
5 Manassas, Virginia 20110-2209, USA. The ATCC deposit was made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained
10 in SEQ ID NO:X, the complement thereof, or the cDNA within the clone deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42°C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the
15 filters in 0.1x SSC at about 65°C.

Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages
20 of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH₂PO₄; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 µg/ml salmon sperm blocking DNA; followed by washes at 50°C with 1XSSPE, 0.1% SDS. In addition, to achieve even
25 lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include
30 Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA+ sequences (such
35 as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a

complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone).

5 The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be
10 single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability
15 or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

 The polypeptide of the present invention can be composed of amino acids joined
20 to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs,
25 as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be
30 branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a
35 nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine,

formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

"SEQ ID NO:X" refers to a polynucleotide sequence while "SEQ ID NO:Y" refers to a polypeptide sequence, both sequences identified by an integer specified in Table 1.

"A polypeptide having biological activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention.)

Polynucleotides and Polypeptides of the Invention

FEATURES OF PROTEIN ENCODED BY GENE NO: 1

The translation product of this gene shares sequence homology with LIM-homeobox domain proteins, such as T-cell translocation protein, which are thought to be important in development and leukemogenesis. In addition, translation product of this gene shares homology with the human breast tumor autoantigen (See Accession No. gil1914877). In one embodiment the polypeptides of the invention comprise the sequence:

MNGSHKDLLPFPASARTPSLPPAPPAQAPLPWKPSGFARISPPPPLAILQYRG
KADHGESGQQLAAAPGDGRLPLLEAVRRLRGQDCGPLSALCHGQLLAQVPVQ
VLLPGAXGDIGTSCYTKSGMILCRNDYIRLFGNSGACSACGQSIPASELVMRA
QGNVYHLKCFTCSTCRNRLVPGDRFHYINGSLFCEHDRPTALINGHLNSLQSN

PLLPDQKVCKVRVMQNACLHLRFVHHRWIPCXFSRQVTFVASTSASSMPLHLL
 (SEQ ID NO:211); MARTR: PSSPFLLLRELPPSLQLRQPRRPFGSRAASLAFHRR
 RLSQYCNIGEKQTMVNPGSSSQPPPVTAGSLSWKRCAGCGGKIADRFLLYA
 (SEQ ID NO:212); LFGNSGACSACGQSIPASELVMRA (SEQ ID NO:213);
 5 HDRPTALINGHLNSLQSNP (SEQ ID NO:214); and/or LYPGDRFHYING (SEQ ID
 NO:215). Polynucleotide fragments encoding these polypeptide fragments are also
 encompassed by the invention.

This gene is expressed primarily in fetal brain, osteosarcoma, IL-1/TNF treated
 synovial, and estradiol treated endometrial stromal cells, and to a lesser extent in
 10 chondrosarcoma, smooth muscle and number of other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as
 reagents for differential identification of the tissue(s) or cell type(s) present in a
 biological sample and for diagnosis of diseases and conditions which include, but are
 not limited to, developmental defects or leukemia. Similarly, polypeptides and
 15 antibodies directed to these polypeptides are useful in providing immunological probes
 for differential identification of the tissue(s) or cell type(s). For a number of disorders
 of the above tissues or cells, particularly of the hematopoietic system and immune
 system, expression of this gene at significantly higher or lower levels may be routinely
 detected in certain tissues and cell types (e.g., brain and other tissue of the nervous
 20 system, bone cells, synovial tissue, endometrial tissue and other reproductive tissue,
 cartilage cells, smooth muscle, and blood cells and cells and tissue of the immune
 system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma,
 urine, synovial fluid or spinal fluid) or another tissue or cell sample or another tissue or
 cell sample or another tissue or cell sample taken from an individual having such a
 25 disorder, relative to the standard gene expression level, i.e., the expression level in
 healthy tissue or bodily fluid or bodily fluid or bodily fluid from an individual not
 having the disorder. Preferred epitopes include those comprising a sequence shown in
 SEQ ID NO. 111 as residues: Met-1 to Cys-9.

The tissue distribution and homology to the LIM-homeodomain containing
 30 proteins, such as T-cell translocation factor, indicates that polynucleotides and
 polypeptides corresponding to this gene are useful for diagnosis and intervention of
 leukemia and other developmental defects. Because of the importance of the LIM-
 homeodomain proteins in development and their correlation to number of leukemic
 diseases, the molecule can be either used as a diagnostic or prognostic indicator for
 35 leukemia progression or a therapeutic target. In addition, polynucleotides and
 polypeptides corresponding to this gene are useful for the detection/treatment of
 neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease,

Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, and autism. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Furthermore, homology to the breast auto-antigen may suggest this gene is useful in the detection, prevention, and or treatment of breast cancer and/or other proliferative disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 2

Translation product of gene has homology to a highly conserved member of the human calpain family of proteases, Calpain large subunit 1 gene (See Accession No.T32454). Calpains are thought to play a defining role in protein regulation, particularly during development. One embodiment for this gene is the polypeptide fragments comprising the following amino acid sequence:

MKYMGGCAKVMCKYYVILYQGLEYP LLXSGDPETSPPWILRADCIVLSSRNFH
 SNXGRLTINKIYVIGGGKYRGEVTNGAK (SEQ ID NO:216);
 MGQSELYSSILRNLGVFLVYTRGGFLLSPLLHGTLTCAHS (SEQ ID NO:217);
 MVLLLLTVASYTVFWMIGDVLDILFLWNFEYTTLY (SEQ ID NO:218);
 MELYNLCPICYFSTVLTTTYIYFVYSQSSXIRMKVP (SEQ ID NO:219);
 MQIVIVLYCVRNKDKKKVCTCSVQTQFFFPIFPILGCLNGCRTQE (SEQ ID
 NO:220); MKYMGGCAKVMCKYYVILYQGLEYP LLX (SEQ ID NO:221);
 LEYPLLXSGDPET SPPWILRADCIVLSSRNFH SNX (SEQ ID NO:222); and/or
 RNFH SNXGRLTINKIY VIGGGKYRGEVTNGAK (SEQ ID NO:223). An
 additional embodiment is the polynucleotide fragments encoding these polypeptide
 fragments.

This gene is expressed primarily in caudate nucleus, dermatofibrosarcoma protuberance and apoptotic T-cells, and to a lesser extent in eosinophils, brain and smooth muscle.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative diseases or immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system or immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., skin, T-cells and other blood

cells and cells and tissue of the immune system, brain and other tissue of the nervous system, and smooth muscle, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in caudate nucleus and apoptic T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for detection or intervention of neurodegenerative diseases and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder or immune disorders, because the elevated level of the molecule in cells undergoing cell death may be the cause or consequence of these degenerative conditions. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or disorders of the cardiovascular system.

FEATURES OF PROTEIN ENCODED BY GENE NO: 3

This gene maps to chromosome 15, and therefore, may be used as a marker in linkage analysis for chromosome 15. One embodiment for this gene is the polypeptide fragments comprising the following amino acid sequence: VTNEMSQGRGKYDFY IGLGLAMSSSIFIGGSFILKKKGLLRLARKGSMRAGQGGHAYLKEWLWWAGL LSMGAGEVANFAAYAFAPATLVTPLGALSVLVSAILSSYFLNERLNLHGKIGCL LSILG STVMVIHAPKEEEIETLNE (SEQ ID NO:224); VTNEMSQGRGKYDFYIGLGLAMSSSIFIGGSFILKKKGLLRLARKGSMRAGQG GHAYLKEWLWWAGLLSMGAGEVANF (SEQ ID NO:225); NFAAYAFAPATLVTPLGALSVLVSAILSSY (SEQ ID NO:226); and/or ERLNLHGKIGCLLSILGSTVMVIHAPKEEEIETLNE (SEQ ID NO:227). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments

This gene is expressed primarily in colon carcinoma cell line, and to a lesser extent in aorta endothelial cells, T-cells, human erythroleukemia cells (HEL), and stromal cells (TF274).

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, colon carcinoma. Similarly, polypeptides and antibodies directed to

these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of colon carcinoma tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., colon, aorta and other vascular tissue, T-cells and other cells and tissue of the immune system, and stromal cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 113 as residues: Asn-191 to Ser-196, Asn-208 to Gly-214.

The tissue distribution in colon carcinoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for detection and intervention of colon carcinoma and/or other tumors. Additionally the significant presence in T-cell populations may indicate the involvement of the function of the gene product in cancer immunosurveillance. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders, in general. The expression in hematopoietic cells and tissues indicates that this protein may play a role in the proliferation, differentiation, and/or survival of hematopoietic cell lineages. Thus, this gene may be useful in the treatment of lymphoproliferative disorders, and in the maintenance and differentiation of various hematopoietic lineages from early hematopoietic stem and committed progenitor cells.

25

FEATURES OF PROTEIN ENCODED BY GENE NO: 4

This gene is expressed primarily in ovary.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive or endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive or endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., ovary and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial

fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 114 as residues:

5 Pro-20 to Ser-25.

The tissue distribution in ovary indicates that polynucleotides and polypeptides corresponding to this gene are useful for assessing reproductive dysfunction or endocrine disorders, because factors secreted by ovary may be involved in reproductive processes, and in cases have global hormonal effects.

10

FEATURES OF PROTEIN ENCODED BY GENE NO: 5

This gene is expressed primarily in tissues in the central nervous system, including pineal gland, frontal cortex, and dura mater, and to a lesser extent in bladder, lung, T-cells and liver.

15 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative diseases, endocrine disorders, and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are
20 useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., tissue of the nervous system, bladder, lung, liver, and T-cells and other cells and tissues of the
25 immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID
30 NO. 115 as residues: Glu-14 to Arg-20.

The primary tissue distribution in the central nerve system indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and intervention of neurodegenerative diseases or endocrinedisorders, because extracellular proteins in these tissues may function as a neurotrophic factor, a matrix
35 protein for tissue integrity, a neuroguidance factor or as a hormone.

FEATURES OF PROTEIN ENCODED BY GENE NO: 6

This gene is expressed primarily in spleen, resting T-cells, colorectal tumor and pancreatic carcinoma, and to a lesser extent in number of tissues including prostate, synovial hypoxia, osteosarcoma, ulcerative colitis, myeloid progenitor cells, lung and placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation, immunosurveillance of cancers, and immune and gastrointestinal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly in carcinogenesis or the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., prostate, synovial tissue, bone cells, colon, myeloid progenitor cells, lung, cells and tissue of the immune system, cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 116 as residues: Arg-29 to Pro-37, Gln-46 to Val-56.

The primary tissue distribution in lymphatic tissues such as T-cells and spleen, as well as tumors and ulcerative tissues indicates that the protein product of this gene may be involved in the immuno response to or immunosurveillance of carcinogenesis and/or inflammatory conditions.

FEATURES OF PROTEIN ENCODED BY GENE NO: 7

The translation product of this gene shares very weak sequence homology with voltage dependent sodium channel protein and Bowman-Birk proteinase inhibitor which is thought to be important in membrane signaling or extracellular signaling cascades. One embodiment for this gene is the polypeptide fragments comprising the following amino acid sequence: RFKTLMTNKSEQDGDSSKTIEISDMKYHIFQ (SEQ ID NO:228); and/or LVEGKLFYAHKVLLVTXSNR (SEQ ID NO:229) (See Accession No. gnl|PID|d1020763 (AB000216)). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments.

This gene is expressed primarily in prostate cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of prostate cancer tissue, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., prostate and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 117 as residues: Glu-30 to Ser-35.

The tissue distribution in the prostate cancer and homology to sodium channel or proteinase inhibitor suggest that polynucleotides and polypeptides corresponding to this gene are useful for the intervention of cancer progression, because the gene product may be involved in multidrug resistance by altering the drug kinetics by serving the function as a channel transporter. Alternatively, the proteinase inhibitor like function may facilitate tumor metastasis. By targeting these functions, either through vaccine or small molecules, therapeutics may be rationally designed to slow the cancer progression.

FEATURES OF PROTEIN ENCODED BY GENE NO: 8

This gene is expressed primarily in ovary and to a lesser extent in the adrenal gland.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, female infertility and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the female reproductive system and the endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., ovary and other reproductive tissue, and adrenal gland, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample

taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 5 The tissue distribution of this gene in ovary and adrenal gland indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment/diagnosis of female infertility, endocrine disorders, ovarian function, amenorrhea, ovarian cancer and metabolic disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 9

- 10 This gene is expressed only in prostate cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate disorders including cancer. Similarly, polypeptides and
15 antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine and male reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., prostate and cancerous and wounded
20 tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 25 The tissue distribution of this gene only in prostate cancerous tissue, indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment/diagnosis of male infertility, metabolic disorders, and prostate disorders including benign prostate hyperplasia and prostate cancer.

FEATURES OF PROTEIN ENCODED BY GENE NO: 10

- 30 This gene is expressed primarily in placenta and to a lesser extent in ovary.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, female infertility, pregnancy disorders, and ovarian cancer. Similarly,
35 polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive

system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., placenta, and ovary and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from
5 an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 120 as residues: Gln-39 to Gly-73.

The tissue distribution of this gene in placenta and ovary indicates that
10 polynucleotides and polypeptides corresponding to this gene are useful for treatment/diagnosis of female infertility, endocrine disorders, fetal deficiencies, ovarian failure, amenorrhea, and ovarian cancer.

FEATURES OF PROTEIN ENCODED BY GENE NO: 11

15 Gene shares homology with the gene for the Human 3' apolipoprotein B SAR element gene Rh32 (See Accession No. T31530).

This gene is expressed primarily in prostate and in the pancreas.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a
20 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate and pancreatic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this gene
25 at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., prostate and pancreas, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an
30 individual not having the disorder.

The tissue distribution of this gene in prostate and pancreas, indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment/diagnosis of male infertility, prostate disorders including benign prostate hyperplasia, prostate cancer, pancreatic cancer, type I and type II diabetes and
35 hypoglycemia. Homology to a known human apolipoprotein may suggest this gene is useful for the detection, prevention, or treatment of various metabolic disorders,

particularly those secondary to lipoprotein disorders such as atherosclerosis, coronary heart disease, stroke, and hyperlipidemias.

FEATURES OF PROTEIN ENCODED BY GENE NO: 12

- 5 Gene has homology to conserved Beta-casein, an abundant milk protein (See Accession No.Q37894).

 This gene is expressed primarily in stomach.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a
10 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the digestive tract and/or mammary glands. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive system
15 and breast, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., mammary tissue, and stomach and other gastrointestinal tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene
20 expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- The tissue distribution of this gene indicates a role in the treatment/diagnosis of digestive disorders including stomach cancer and ulceration. Furthermore, the homology to conserved beta-casein may indicate this gene as having utility in the
25 diagnosis and prevention of mammary gland disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 13

 This gene is expressed in brain and lung.

- Therefore, polynucleotides and polypeptides of the invention are useful as
30 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative disease states, behavioral abnormalities and pulmonary disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification
35 of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, nervous, and pulmonary systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell

types (e.g., brain and other tissue of the nervous system, and lung, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition it could be used in the detection and treatment of pulmonary disease states such as lung lymphoma or sarcoma formation, pulmonary edema and embolism, bronchitis and cystic fibrosis.

FEATURES OF PROTEIN ENCODED BY GENE NO: 14

This gene is expressed exclusively in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment/detection of immune disorders such as arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Additionally, the expression in hematopoietic cells and tissues indicates that this protein may play a role in the proliferation, differentiation, and/or survival of hematopoietic cell lineages. Thus, this gene may be useful in the treatment of lymphoproliferative disorders, and in the maintenance and differentiation of various hematopoietic lineages from early hematopoietic stem and committed progenitor cells.

FEATURES OF PROTEIN ENCODED BY GENE NO: 15

This gene is expressed primarily in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as
5 reagents for differential identification of the tissue(s) or cell type(s) present in a
biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, immune disorders. Similarly, polypeptides and antibodies directed to
these polypeptides are useful in providing immunological probes for differential
10 identification of the tissue(s) or cell type(s). For a number of disorders of the above
tissues or cells, particularly of the immune system, expression of this gene at
significantly higher or lower levels may be routinely detected in certain tissues and cell
types (e.g., T-cells and other cells and tissue of the immune system, and cancerous and
wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal
15 fluid) or another tissue or cell sample taken from an individual having such a disorder,
relative to the standard gene expression level, i.e., the expression level in healthy tissue
or bodily fluid from an individual not having the disorder. Preferred epitopes include
those comprising a sequence shown in SEQ ID NO. 125 as residues: Ala-46 to Asp-51.

The tissue distribution indicates that polynucleotides and polypeptides
corresponding to this gene are useful for the diagnosis and treatment of immune
20 disorders including: leukemias, lymphomas, auto-immunities, immunodeficiencies
(e.g. AIDS), immuno-suppressive conditions (transplantation) and hematopoietic
disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 16

25 This gene is expressed primarily in endometrial tumors.

Therefore, polynucleotides and polypeptides of the invention are useful as
reagents for differential identification of the tissue(s) or cell type(s) present in a
biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, cancer, particularly endometrial. Similarly, polypeptides and antibodies
30 directed to these polypeptides are useful in providing immunological probes for
differential identification of the tissue(s) or cell type(s). For a number of disorders of
the above tissues or cells, particularly of the female reproductive system, expression of
this gene at significantly higher or lower levels may be routinely detected in certain
tissues and cell types (e.g., endometrial cells and other reproductive cells or tissue, and
35 cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial
fluid or spinal fluid) or another tissue or cell sample taken from an individual having

such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of ovarian and
5 other endometrial cancers, as well as reproductive dysfunction, prenatal disorders or fetal deficiencies.

FEATURES OF PROTEIN ENCODED BY GENE NO: 17

This gene is expressed primarily in a variety of osteoclastic cells: osteoclastoma
10 stromal cells, osteosarcoma, chondrosarcoma and stromal cell culture. To a lesser extent, it is also seen in a variety of fetal and embryonic cell and tissue types.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are
15 not limited to, bone cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal and developmental systems, expression of this gene at
20 significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., bone cells, cartilage, and stromal cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those
25 comprising a sequence shown in SEQ ID NO. 127 as residues: Gln-34 to Gln-41, Asn-76 to Lys-82, Ser-85 to Lys-91.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and detection of a variety disorders and conditions affecting bone and the skeletal system, including: osteoporosis, fracture,
30 osteosarcoma, osteoclastoma, chondrosarcoma, ossification and osteonecrosis, arthritis, tendonitis, chondromalacia and inflammation.

FEATURES OF PROTEIN ENCODED BY GENE NO: 18

This gene is expressed primarily in smooth muscle.

35 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, cardiovascular disorders including lymphatic system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular and lymphatic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., smooth muscles, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of conditions and pathologies of the cardiovascular system: heart disease, restenosis, atherosclerosis, stoke, angina, thrombosis, and wound healing.

FEATURES OF PROTEIN ENCODED BY GENE NO: 19

The translation product of this gene shares sequence homology with 5'-nucleotidase (See Accession No. 2668557) as well as the gene for alpha-1 collagen type X (See Accession No. gb|X67348|MMCOL10A). One embodiment for this gene is the polypeptide fragments comprising the following amino acid sequence:

MAQHFSLAACDVVGFDLDHTLCRYNLPESAPLIYNSFAQLVKEKGYDKELLN
 VTPEDWDFCCKGLALDLEDGNFLKLANNGTVLRASHGTKMMTPEVLAEAYG
 KKEWKHFLSDTGMACRSGKYFYDNYFDLPGALLCARVVDYLTCLNNGQKT
 25 FDFWKDIVAAIQHNYKMSAFKENCGIYFPEIKRDPGRYLHSCPEVKKWLRQL
 KNAGKILLITSSHSDYCRLLCEYILGNDFTDLFDIVITNALKPGFFSHLPSQRPF
 RTLENDEEQEALPSLDKPGWYSQGNVHL YELLKKMTGKPEPKVVYFGDSMH
 SDIFPARHYSNWETVLILEELRGDEGTRSQRPEESEPLEKKGKYEGPKAKPLNT
 SSKKWGSFFIDSVLGLENTEDSLVYTWSCKRISTYSTIAIPSEIAIAELPLDYKFT
 30 RFSSSNSKTAGYYPNPPLVLSSDETLISK (SEQ ID NO:233); and/or
 TSSHSDYCRLLCEYILGNDFTDLFDIV (SEQ ID NO:234). An additional
 embodiment is the polynucleotide fragments encoding these polypeptide fragments.
 Additionally, another embodiment for this gene is the polynucleotide fragments
 comprising the following sequence:

35 CCTTAAAAGCTGACATTTTATAATTGTGTTGTATAGCAGCAACTATATCCTTC
 CAAAAATCAAATGTTTTTTGACCATTGTTTCAGTT (SEQ ID NO:230);
 CCTTAAAAGCT GACATTTTATAATTGTGTTGTATAGCA (SEQ ID NO:231);

and/or CTTCCAAAAA TCAAATGTTTTTTGACCATTGTTTCAGTT (SEQ ID NO:232). An additional embodiment is the polypeptide fragments encoded by these polynucleotide fragments. This gene maps to chromosome 6, and therefore, may be used as a marker in linkage analysis for chromosome 6.

5 This gene is expressed primarily in prostate and smooth muscle.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate cancer and cardiovascular disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate and cardiovascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., prostate, and smooth muscle, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

15 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of prostate cancer and other disorders. In addition the expression in smooth muscle would suggest a role for this gene product in the treatment and diagnosis of cardiovascular disorders such as hypertension, restenosis, atherosclerosis, stroke, angina, thrombosis, and other aspects of heart disease and respiration.

25

FEATURES OF PROTEIN ENCODED BY GENE NO: 20

This gene is expressed primarily in endometrial tissue and to a lesser extent in synovium.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endometrial cancer and arthritis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and skeletal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endometrial tissue and other reproductive tissue,

and synovial tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 130 as residues: Ser-19 to His-24, Pro-36 to Arg-43, Ala-61 to Gly-67, Pro-86 to Ala-95.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of endometrial cancers, as well as reproductive and developmental disorders (fetal deficiencies and other pre-natal conditions). In addition the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular the connective tissues (e.g. arthritis, trauma, tendonitis, chondromalacia and inflammation).

FEATURES OF PROTEIN ENCODED BY GENE NO: 21

This gene maps to chromosome 6, and therefore, may be used as a marker in linkage analysis for chromosome 6.

This gene is expressed primarily in keratinocytes, fetal tissue (especially fetal brain) and leukocytic cell types and tissues (e.g. B-cell, macrophages, Jurkat T-Cell, T cell helper cells, spleen, thymus and lymphoma).

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, integument and immune systems, as well as developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, immune and central nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., keratinocytes, brain and other tissue of the nervous system, differentiating tissue, leukocytes and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders including: leukemias, lymphomas, auto-immunities, immunodeficiencies (e.g. AIDS), immuno-suppressive conditions (transplantation) and hematopoietic disorders. Expression in keratinocytes would suggest a role for the gene product in the diagnosis treatment of skin disorders such as cancers (melanomas), eczema, psoriasis, wound healing and grafts. In addition the expression in fetal brain might implicate this gene product in the detection and treatment of developmental and neurodegenerative diseases of the brain and nervous system: behavioral or nervous system disorders, such as depression, schizophrenia, Alzheimer's disease, Parkinson's disease, Huntington's disease, mania, dementia, paranoia, addictive behavior and sleep disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 22

Translation product of this gene shares significant homology with the conserved YME1 PROTEIN from *Saccharomyces cerevisiae*, which is a putative ATP-dependent protease thought to regulate the assembly of key respiratory chains within the mitochondria (See Accession No. P32795). Preferred polypeptide fragments comprise the following amino acid sequence:

MKTKNIPEAHQDAFKTGFAEGFLKAQALTQKTNDLRRTRLILFVLLLFGIYGL
 LKNPFLSVRFRTTTGLDSAVDPVQMKNVTFEHVKGVEEAKQELQEVVEFLKNP
 QKFTILGGKLPKGILLVGPPGTGKTLLARAVAGEADVPFYYASGSEFDEMFGV
 VGASRIRNLFREAKANAPCVIFIDELDSVGGKRIESPMHPYSRQTINQLLAEMD
 GFKPNEGVIIGATNFPEALDNALIRPGRFDMQVTVPDPVKGRTEILKWYLNK
 IKFDXSVDPEILARGTVGFSGAELENLVNQAALKA AVDGKEMVTMKELGVFQR
 QNSNGA (SEQ ID NO:235); MKTKNIPEAHQDAFKTGFAEG (SEQ ID NO:236);
 PVQMKNVTFEHVKGVEEAKQELQ (SEQ ID NO:237);
 SRQTINQLLAEMDGFKPN EGVII (SEQ ID NO:238); and/or
 FSGAELENLVNQAALKA AVDGKEM (SEQ ID NO:239). Also preferred are
 polynucleotide fragments encoding these polypeptide fragments.

This gene is expressed primarily in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoietic systems,

expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders including: leukemias, lymphomas, auto-immunities, immunodeficiencies (e.g. AIDS), immuno-suppressive conditions (transplantation) and hematopoietic disorders. Furthermore, the homology of this gene indicates that it may play an important role in disorders affecting metabolism.

15 **FEATURES OF PROTEIN ENCODED BY GENE NO: 23**

This gene is expressed primarily in human chronic synovitis.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, synovial and other inflammatory disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the synovial tissue and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., synovial tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that the protein product of this gene are useful for study, diagnosis and treatment of inflammatory disorders such as chronic synovitis.

FEATURES OF PROTEIN ENCODED BY GENE NO: 24

This gene is expressed primarily in pituitary, breast cancer, and bone marrow; and to a lesser extent in breast, prostate, uterine cancer and cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine, reproductive disorders and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive, metabolic and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., pituitary, mammary tissue, bone marrow, prostate, reproductive tissue, uterus, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 134 as residues: Asp-32 to Gln-38, Lys-88 to Ile-97.

The tissue distribution indicates that the protein products of this gene are useful for the study, treatment and diagnosis of various endocrine disorders, reproductive diseases and disorders and cancers.

FEATURES OF PROTEIN ENCODED BY GENE NO: 25

The translation product of this gene shares sequence homology with androgen withdrawal apoptosis protein in rat which is thought to be important in programmed cell death. Preferred polypeptides encoded by this gene comprise the following amino acid sequence:

LPMWQVTAFLDHNIVTAQTTWKGLWMSCVVQSTGHMQCKVYDSVLALSTEV
 QAARALTVSAVLLAFVALFVTLAGAQCCTTCVAPGPAKARVALTGGVLYLFCGL
 LALVPLCWFANIVVREFYDPSVPVSQKYELGAXLYIGWAATALLMVGGLCC
 GAWVCTGRPDLSFPVKYSAPRRPTATGDYDKKNYV (SEQ ID NO:240). This polypeptide is expected to contain multiple transmembrane domains. The extracellular portion of the polypeptide is expected to comprise residues 1-51 of the foregoing amino acid sequence. Therefore, particularly preferred polypeptides encoded by this gene comprise residues 1-51 of the foregoing amino acid sequence. Polynucleotides encoding the foregoing polypeptides are also provided.

This gene is expressed primarily in human adult pulmonary and brain (striatum) tissue and to a lesser extent in thymus, synovium and testis.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, reproductive, metabolic, and neurodegenerative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive, nervous, respiratory and metabolic systems expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., thymus, synovial tissue, testis and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to androgen withdrawal apoptosis rat gene protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of disorders in which the mechanism controlling programmed cell death is instrumental. This could include reproductive, neurodegenerative, and various metabolic disorders and diseases such as cancer.

FEATURES OF PROTEIN ENCODED BY GENE NO: 26

The translation product of this gene shares homology with both ubiquitin and a G-protein coupled receptor TM3 consensus polypeptide (see Genbank accession Nos. gnllPIDle331456 (AJ000657) and R50664, respectively). Preferred polypeptides encoded by this gene comprising the following amino acid sequence:
 LHYFALSFVLILTEICLVSSGMGF (SEQ ID NO:241);
 QLRNGIPPGRKALFCSGKPR LFTLGQGRTCA (SEQ ID NO:242); and/or
 WSGLWVTTWNGSSGERTPSPWRRK RASQSAGRIASWMSF (SEQ ID NO:243).
 An additional embodiment is polynucleotides encoding these polypeptides. This gene maps to chromosome 1, and therefore, may be used as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in activated T cells and to a lesser extent in CD34 depleted buffy coat.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and hemopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hemopoietic and immune system,

expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other blood cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 136 as residues: Thr-15 to His-21, Gly-30 to Lys-39, Arg-113 to Met-118, Arg-178 to Ala-187.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. Furthermore, the homology to G-coupled proteins as well as to ubiquitin may implicate this gene as being important in regulation of gene expression and protein sorting - both of which are vital to development and wound healing models. Therefore, the gene may provide utility in the diagnosis, prevention, and/or treatment of various developmental disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 27

This gene is expressed primarily in activated T cells and to a lesser extent in fetal kidney.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, developmental and metabolic diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and metabolic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from

an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides
 5 corresponding to this gene are useful for the study and treatment of diseases and disorders of the immune, metabolic, and endocrine systems; such as renal diseases and T cell dysfunctions. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency
 10 diseases such as AIDS, and leukemia.

FEATURES OF PROTEIN ENCODED BY GENE NO: 28

The translation product of this gene shares sequence homology with Cystatin-related epididymal specific protein in mouse which is thought to be important in
 15 reproductive system function/regulation (See Genbank accession no.bbsl18813). Based on the structural similarity between these proteins, the translation product of this clone, hereinafter "Cystatin G", is expected to share biological activities with cystatin related proteins and other cysteine protease inhibitors. Such activities are known in the art and are described elsewhere herein. Preferred polypeptides encoded by this gene
 20 comprising the following amino acid sequence:
 MPRCRWLSLILLTIPLALVARKDPKKNETGVLRLKLPVNASNANVKQCLWFA
 MQEYNKESEDKYVFLVVKTLQAQLQVTNLLEYLIDVEIARSDCRKPLSTNEICAI
 QENSKLKRKLSCSFLVGALPWNGEFTVMEKKCEDA (SEQ ID NO:246);
 ARKDPKKNETGVLRLKLPVNASNANVKQCLWFAMQEYNKESEDKYVFLVVK
 25 TLQAQLQVTNLLEYLIDVEIARSDCRKPLSTNEICAIQENSKLKRKLSCSFLVGA
 LPWNGEFTVMEKKCEDA (SEQ ID NO:248);
 CLWFAMQEYNKESEDKYVFLVVKTLQAQLQVTNLLEYLIDVEIARSDCRKPLST
 NEICAIQENSKLKRKLSCSFLVGALPWNGEFTVMEKKC (SEQ ID NO:247);
 EYNKESEDKYVFLV (SEQ ID NO:244); and/or IDVEIARSDCRKPL (SEQ ID
 30 NO:245). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments. Preferred cystatin polypeptide fragments are shown to be active in the following assays: The methods used for active site titration of papain, titration of the molar enzyme inhibitory concentration in cystatin G preparations, and for determination of equilibrium constants for dissociation (K_i) of complexes between
 35 cystatin G and cysteine peptidases are described in detail in Hall et al., Biochem. J., 291:123-29 (1993) and Abrahamson, Methods Enzymol., 244:685-700 (1994), both of which are hereby incorporated herein by reference. The enzymes used for equilibrium

assays are papain (EC 3.4.22.2; from Sigma, St Louis, MO) and cathepsin B (EC 3.4.22.1; from Calbiochem, La Jolla, CA). The fluorogenic substrate used was Z-Phe-Arg-NHMec (10 mM; from Bachem Feinchemikalien, Bubendorf, Switzerland) and the assay buffer was 100 mM Na-phosphate buffer (pH 6.5 and 6.0 for papain and cathepsin B, respectively), containing 1 mM dithiothreitol and 2 mM EDTA. Steady state velocities are measured and K_i values were calculated according to Henderson, Biochem J., 127:321-333 (1972), incorporated herein by reference. Corrections for substrate competition are made using K_m values of 150 μ M for cathepsins B (Barrett and Kirschke, Methods Enzymol., 80:535-561 (1981) and 60 μ M for papain (Hall et al., Biochem. J., 291:123-29 (1992)), both of which are hereby incorporated herein by reference.

This gene is expressed primarily in human testes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive disorders and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., testis and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 138 as residues: Arg-21 to Thr-29.

The tissue distribution and homology to cystatin-related epididymal specific protein-mouse indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of reproductive diseases and disorders. Cysteine proteinase inhibitors of the cystatin superfamily are ubiquitous in the body and are generally tight-binding inhibitors of papain-like cysteine proteinases, such as cathepsins B, H, L, S, and K (for review, see Ref. 1). They should therefore serve a protective function to regulate the activities of such endogenous proteinases, which otherwise may cause uncontrolled proteolysis and tissue damage. Cysteine proteinase activity can normally not be measured in body fluids, but can be detected extracellularly in conditions like endotoxin-induced sepsis (2), metastasizing cancer (3), and at local inflammatory processes in rheumatoid arthritis (4), purulent bronchiectasis

(5) and periodontitis (6), which indicates that a tight cystatin regulation is a necessity in the normal state. A deficiency state in which the levels of the intracellular cystatin, cystatin B, are lowered due to mutations has recently been shown to segregate with a form of progressive myoclonus epilepsy (7), which points to additional specialized functions of cystatins. Moreover, results showing that chicken cystatin inhibits polio virus replication (8), human cystatin C inhibits corona- and herpes simplex virus replication (9,10), and human cystatin A inhibits rhabdovirus-induced apoptosis (11) in cell cultures indicates that cystatins play additional roles in the human defense system. The cystatins constitute a superfamily of evolutionary related proteins, all composed of at least one 100-120 residue domain with conserved sequence motifs (12). The previously well characterized single-domain human members of superfamily could be grouped in two protein families. The Family 1 members, cystatins (or stefins) A and B, contain approximately 100 amino acid residues, lack disulfide bridges, and are not synthesized as preproteins with signal peptides. The Family 2 cystatins (cystatins C, D, S, SN, and SA) are secreted proteins of approx. 120 amino acid residues (Mr 13,000-14,000) and have two characteristic intrachain disulfide bonds. Recently, we identified an additional human cystatin superfamily member by EST1 sequencing in epithelial cell derived cDNA libraries which we named cystatin E (13). The same cystatin was independently discovered by differential display experiments as a mRNA species down-regulated in breast tumor tissue, but present in the surrounding epithelium and reported under the name cystatin M (14). Cystatin E/M is an atypical, secreted low-Mr cystatin in that it is a glycoprotein and just shows 30-35% sequence identity in alignments with the human Family 2 cystatins, which shows that additional cystatin families are yet to be identified (13). The cystatin E/M gene has been localized to chromosome 2 (15), whereas all human Family 2 cystatin genes are clustered on the short arm of chromosome 20 (16), which further stresses that cystatin E/M is just distantly related to the other secreted human low-Mr cystatins.

FEATURES OF PROTEIN ENCODED BY GENE NO: 29

The translation product of this gene shares sequence homology with the leukocyte-associated Ig-like receptor-1, putative inhibitory receptor which is thought to be important in regulation of various physiological functions (See Accession No. gi2352941 (AF013249). Preferred polypeptides encoded by this gene comprise the following amino acid sequence:

DSPDTEPGSSAGPTQRPSDNSHNEHAPASQGLKAEHLYILIGVS (SEQ ID NO:249); HRQNQIKQGPPRSKDDEQKPQRPDLAVDVLERTADKATVNGL PEKDRETDTSALAAGSSQEVTYAQLDHWALTQRTARAVSPQSTKPMAESITYAA

VARH (SEQ ID NO:250);

MSPHPTALLGLVLCLAQTIHTQEEDLPRPSISAEPGTVIPLGSHVTFVCRGPVGV
QTFRLERESRSTYNDTEDVSQASPSESEARFRIDSVSEGNAGPYRCIYYKPKW
SEQSDY (SEQ ID NO:251); TALLGLVLCLAQTIHTQE (SEQ ID NO:252);

- 5 LPRPSISAEPGTVI (SEQ ID NO:253); CRGPVGVQTFRLERE (SEQ ID NO:254);
and/or VLERTADKATVNGLPEKDRETDTSALAAGSS (SEQ ID NO:255).

Additional embodiments of the invention include polynucleotides encoding these polypeptides.

- 10 This gene is expressed primarily in macrophages and T-cells and to a lesser extent in human fetal heart.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, inflammatory, and immune disorders. Similarly,
- 15 polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the growth and inflammatory systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., macrophages, T-cells
- 20 and other cells and tissue of the immune system, heart, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those
- 25 comprising a sequence shown in SEQ ID NO. 139 as residues: His-20 to Arg-28, Glu-61 to Val-74, Ser-78 to Ala-84, Lys-105 to Ser-117.

- The tissue distribution and homology to putative inhibitory receptor indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis and treatment of functional disorders of the developing fetal heart;
- 30 including circulatory and vascular; and inflammatory disorders. In addition expression in macrophages and lymphocytes indicates a role in the treatment/detection of immune disorders including disorders such as arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia.

35 FEATURES OF PROTEIN ENCODED BY GENE NO: 30

The translation product of this gene shares sequence homology with erythroid cell specific transcription factor- murine which is thought to be important in normal

physiological function of erythroid cells. In addition, the translation product of this gene also shares homology with the conserved 3-phosphoglycerate dehydrogenase gene which is essential component of metabolic biosynthetic pathways. Preferred polypeptides comprise the following amino acid sequence:

- 5 MNTPNGNSLSAAELTCGMIMCLARQIPQATASMKDGKWERKKFMGTELNGK
 TLGILGLGRIGREVATRMQSFGMKTIGYDPIISPEVSASFVQQLPLEEIWPLCDF
 ITVHTPLLSTTGLLNDNTFAQCKKGVRVVCARGGIVDEGALLRALQSGQCA
 GAALDVFTTEPPRDRAVDHENVISCPHLGASTKEAQSRCGEEIAVQFVDMVK
 GKSLTGVVNAQALTSFSPHTKPWIGLAEALGTLMRAWAGSPKGTIQVITQGT
 10 SLKNAGNCLSPAVIVGLLKEASKQADVNLVNAKLLVKEAGLNVTTSHSPAAPG
 EQGFGECLLAVALAGAPYQAVGLVQGTPVLQGLNGAVFRPEVPLRRDLPLLL
 FRTQTSDPAMLPTMIGLLAEAGVRLLSYQTSLSVDGETWHVMGISSLLPSLEAW
 KQHVTEAFQFHF (SEQ ID NO:256); MAFANLRKVLISDSLDPCCRKILQ (SEQ ID
 NO:257); GGLQVVEKQNL SKEELIA (SEQ ID NO:258);
 15 MCLARQIPQATASMKDGKWERKKFMGTEL (SEQ ID NO:259);
 ALTSFSPHTKPWIGLAEALGTLMRAWAG (SEQ ID NO:260); and/or
 EVPLRRDLPLLLFRTQTSDPAMLPTMIGLLAEAGVR (SEQ ID NO:261). Also
 preferred are polynucleotide fragments encoding these polypeptides. This gene maps to
 chromosome 1, and therefore, may be used as a marker in linkage analysis for
 20 chromosome 1.

This gene is expressed primarily in IL-1 induced smooth muscle and fetal kidney and to a lesser extent in myeloid progenitor cell line and bone marrow.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a
 25 biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hemopoietic, and cardiovascular disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hemopoietic and
 30 immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., smooth muscle, kidney, myeloid progenitor cells, bone, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene
 35 expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 140 as residues: Met-1 to Asn-7, Met-33 to Lys-42,

Asn-123 to Cys-130, Glu-169 to Asp-174, Ser-192 to Gly-201, Thr-266 to Asn-273, Pro-318 to Phe-323.

The tissue distribution and homology to erythroid cell specific murine transcription factor indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of disorders and diseases involving the hemopoietic and immune systems; the maturation of progenitor cells; and the development of various smooth muscle tissues (heart, etc.). In addition, homology to a key biosynthetic protein implicates this the protein product of this gene as being important in metabolism. Therefore, the protein may show utility in the diagnosis, prevention, and/or treatment of metabolic disorders and conditions.

FEATURES OF PROTEIN ENCODED BY GENE NO: 31

This gene is expressed primarily in human adult testes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive disorders, particularly of the male genitalia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 141 as residues: Met-1 to Pro-8, Ser-45 to Thr-50.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis, treatment, and possibly prevention of various male reproductive disorders and diseases including male impotence, failed libido and male secondary sex characteristics, infertility, and testicular cancer.

FEATURES OF PROTEIN ENCODED BY GENE NO: 32

This gene is expressed primarily in human adult testis.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive disorders and cancers of the male reproductive system.

- 5 Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., testis and other reproductive
10 tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 15 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis, treatment, and possibly prevention of various male reproductive disorders and diseases including male impotence, failed libido and male secondary sex characteristics, infertility, and testicular cancer.

20

FEATURES OF PROTEIN ENCODED BY GENE NO: 33

- The translation product of this gene shares homology to the W09D10.1 protein of *Caenorhabditis elegans*. In addition, the gene also shares homology with the human protein hRIP, a protein known to be critical for HIV replication (See Accession
25 Nos.gnllPIDle1186472 and W12713). Preferred polypeptides encoded by this gene comprise the following amino acid sequence:
- MDLLGLDAPVACSIANSKTSNTLEKDLLASVPSPSSSGSRKVVGSMPTAGSA
GSVPENLNLFPPEPGSKSEEIGKKQLSKDSILSLYGSQTXQMPTQAMFMAPAQM
AYPTAYPSFPGVTPPNSIMGSMMPPPVGMVAQPGASGMVAPMAMPAGYMGG
30 MQASMMGVPNGMMTTQQAGYMAAGMAAMPQTVYGVQPAQQLQWNLTQMTQ
QMAGMNFYGANMMNYGQSMMSGNGQAANQTLSPQMWKFGTRFLANLLE
EDNKFCADCQSKGPRWASWNIGVFICIRCAXIHRNLGVHISR VKSVNLDQWTQ
VQIQ (SEQ ID NO:267); MQXMGNGKANRLYEAYLPETFRPQIDPAVEGFIR
DXYE (SEQ ID NO:268); EEDNKFCADCQSKGPRWASWN (SEQ ID NO:263);
35 GVFICIRCAXIHR NLGVHIS (SEQ ID NO:264); and/or SVNLDQWTQVQIQCMQX
MGNGKA (SEQ ID NO:265). Polynucleotides encoding these polypeptides are also provided.

This gene is expressed primarily in lymphoid tumors.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and inflammatory disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, hematopoietic and inflammatory, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., lymphoid tissue and other tissue and cells of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 143 as residues: Cys-21 to Trp-28.

The tissue distribution indicates that the protein products of this gene are useful for study, diagnosis and treatment of various immune disorders and diseases, including self-recognition and rejection functions of the immune system, hematopoietic disorders, and inflammatory disorders. Homology to the W09D10.1 of *C.elegans* and the hRIP implicates this gene as playing a role as an essential receptor for host-viral interactions including, but not limited to retroviral infections such as AIDS.

FEATURES OF PROTEIN ENCODED BY GENE NO: 34

The translation product of this gene shares homology to an Arabidopsis thaliana recombination and DNA-damage resistance/repair protein (See Accession No.gil166694). Preferred polypeptides encoded by this gene comprise the following amino acid sequence:

KYGKVGKCVIFEIPGAPDDEAVRIFLEFERVESAIKAVVDLNGRYFGGRVVKAC
FYNLDKFRVLDLA (SEQ ID NO:269); KAVDLGRYFGGR (SEQ ID NO:270);
and/or EAVRIFFRE (SEQ ID NO:271). Polynucleotides encoding these polypeptides are also provided.

This gene is expressed primarily in ovarian and other cancers.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer, particularly of the female reproductive system. Similarly,

polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely
 5 detected in certain tissues and cell types (e.g., ovaries and other reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the
 10 disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 144 as residues: Thr-11 to Trp-19, Ala-40 to Gln-47, Lys-58 to Arg-66, Asp-98 to Lys-110, Arg-114 to Glu-121.

The tissue distribution in tumors of ovarian origins combined with the homology to a known DNA damage repair enzyme indicates that polynucleotides and
 15 polypeptides corresponding to this gene are useful for diagnosis and intervention of tumors. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.

FEATURES OF PROTEIN ENCODED BY GENE NO: 35

20 Translation product of this gene shares homology with human stomatin, intestinal surface antigens, as well as protein F30A10.5 of *Caenorhabditis elegans* (See Accession No.gnllPIDle276130). Preferred polypeptides encoded by this contig comprise the following amino acid sequence: RMGRFHRILEPGLNILIPVLDRIRYVQ
 25 SLKEIVINVPEQSAVTLDNVTQLQIDGVLRLIMDPYKASYGVEDPEYAVTQLAQT
 TMRSELGKLSLDKVFRRERESLNASIVDAINQAADCWGIRCLRYEIKDIHVPPRV
 KESMQMQVEAERRKRATVLESEGTRESAINVAEGKKQAQILASEAEKAEQINQA
 AGEASAVLAKAKAKAEAIRILAAALTQHNGDAAASLTVAEQYVSFAFSKLAKDS
 NTILLPSNPGDVTSMVAQAMGVYGALTKAPVPGTPDSLSSGSSRDVQGTDSL
 DEELDRVKMS (SEQ ID NO:272); ASYGVEDPEYAVTQLAQT MRSELGK (SEQ
 30 ID NO:273); MQMQVEAERRKRATVLESEGTRESAIN (SEQ ID NO:274);
 LTVAEQYVSFAFSKLAKDSNTILLPSN (SEQ ID NO:275), and/or
 LLGATAPLVSLVPEVAAAVGNAGARGAXHWGPFAEGLSTGFWPR SARASSGL
 PRNTVVLFPQQEAWVVE (SEQ ID NO:276). Polynucleotides encoding these
 polypeptides are also provided.

35 This gene is expressed primarily in activated T-cells and to a lesser extent in other cell types.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 145 as residues: Arg-23 to Pro-33, Pro-184 to Ser-189, Ala-196 to Arg-201, Glu-208 to Ser-213, Glu-230 to Ile-237, Gly-326 to Leu-331, Gly-334 to Gln-340.

The tissue distribution indicates that the protein products of this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, the homology to known intestinal antigens may suggest that the protein is important in the diagnosis, treatment, and/or prevention of gastrointestinal disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 36

Translation product of this gene has homology to a human estrogen receptor variant from human breast cancer. Preferred polypeptides encoded by this gene comprise the following amino acid sequence: RMWRNGTHFWECKIVQPLWK TVWWFPRKLSIELPENLAILIGTYFK (SEQ ID NO:277); and/or LKRHFPKEANK HVKRCSTSLDIREIQIKIMRY (SEQ ID NO:278). Polynucleotides encoding these polypeptides are also provided.

This gene is expressed primarily in ulcerative colitis.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, intestinal ulcers, inflammatory conditions and cancers, particularly of the breast. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the gastrointestinal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., colon and other gastrointestinal tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in colon and breast origins indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of tumors or other conditions within these tissues, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.

20 FEATURES OF PROTEIN ENCODED BY GENE NO: 37

This gene is expressed primarily in epithelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers and skin disorders, particularly melanoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin and other epithelia, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 147 as residues: Met-1 to Tyr-6.

The tissue distribution in epithelial tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of

tumors of this tissue. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

5 **FEATURES OF PROTEIN ENCODED BY GENE NO: 38**

This gene is expressed primarily in adult retina.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are
10 not limited to, diseases of the eye. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the eye, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., epithelial
15 cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID
20 NO. 148 as residues: Cys-14 to Lys-21.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the eye.

25 **FEATURES OF PROTEIN ENCODED BY GENE NO: 39**

This gene is expressed primarily in bone marrow and fetal liver.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are
30 not limited to, hemopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hemopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell
35 types (e.g., bone marrow and liver, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard

gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the hemopoietic system.

FEATURES OF PROTEIN ENCODED BY GENE NO: 40

This gene is expressed primarily in lymph node, fetal liver and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hemopoietic diseases and disorders of the CNS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hemopoietic and CNS, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., lymphoid tissue and other tissue of the immune system, liver, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that the protein products of this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders. Expression in embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Additionally, the expression in hematopoietic cells and tissues indicates that this protein may play a role in the proliferation, differentiation, and/or survival of hematopoietic cell lineages. Thus, this gene may be useful in the treatment of lymphoproliferative disorders, and in the maintenance and differentiation of various hematopoietic lineages from early hematopoietic stem and committed progenitor cells. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, and autism. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental

disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system.

FEATURES OF PROTEIN ENCODED BY GENE NO: 61

- 5 The translation product of this gene shares sequence homology with fibropellin and epidermal growth factors which are thought to be important in growth and regeneration of epidermal cells (See Genbank Accession Nos. W11719 and gil310660). Preferred polypeptides comprise the following amino acid sequence:
- 10 GTRPGESHANDLECSGKGKCTTKPSEATFSCTCEEQYVGTFCEEYDACQRKPC
QNNASCIDANEKQDGSNFTCVCLPGYTGELCQSKIDYCLDPCRNGATCISSLS
GFTQCQCEGYFGSACEEKVDPCASSPCQNNGTCYVDGVHFTCNCSPGFTGPTC
AQLIDFCALSPCAHGTCRSVGTSYKCLCDPGYHGLYCEEEYNECLSAPCLNAA
TCRDLVNGYECVCLAEYKGTHCELYKDPCANVSCLNGATCDS DGLNGTCICA
PGFTGEECDIDINECDSPCHHGGSCLDQPNGYNCHCPHGWWVGANCEIHLQW
15 KSGHMAESLTN (SEQ ID NO:279); GKCTTKPSEATFSCTCEEQYVGTF (SEQ
ID NO:280); CAHG TCRSVGTSYKCLCDPGYH (SEQ ID NO:281); and/or
CANVSCLNGATCDS DGLNG TCICAPGFTGEECD (SEQ ID NO:282).
Polynucleotides encoding these polypeptides are also provided.

- 20 This gene is expressed primarily in brain and kidney and to a lesser extent in several other tissues and organs.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the neural and renal systems, particularly growth disorders
25 such as cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neural and renal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., brain and other
30 tissue of the nervous system, and kidney, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 35 The tissue distribution and homology to epidermal growth factor indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of growth disorders especially in the neural and renal systems. In

addition, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, and autism.

- 5 In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system

FEATURES OF PROTEIN ENCODED BY GENE NO: 42

- 10 This gene is expressed primarily in brain, kidney and stromal cells.

- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the CNS and hemopoietic system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hemopoietic, renal and central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., brain and other tissue of the nervous system, kidney, and stromal cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 152 as residues: Lys-71 to Trp-76, Glu-99 to Gly-108, Arg-142 to Ser-149.
- 15
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- The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, and autism. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include
- 30
35

bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product is thought to be involved in lymphopoiesis, therefore, it can be used in immune disorders to modulate infection, inflammation, allergy, immunodeficiency, etc.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 43

The preferred polypeptide encoded by this gene comprise the following amino acid sequence: MAQNKDLAGRLPAGPRGMGTALKLLLGAGAVAYGVRESVFT
VEGGHRAIFFNRIGGVQQDTILAEGLHFRIPWFQYPIIYDIRARPRKISSPTGSKD
10 LQMVNISLRVLSRPNAQELPSMYQRLGLDYEERVLPSIVNEVLKSVVAKFNASQ
LITQRAQVSLIRRELTERAKDFSLLDDVAITELSFSSREYTA AVEAKQVAQQEAQ
RAQFLVEKAKQEQKIVQAEGEAEAAKMLGEALSKNPGYIKLRKIRAAQNIS
KTIATSQNRIYLTADNLVLNLQDESFTRGSDSLIKGKK (SEQ ID NO:283). The
gene product above share sequence similarity with prohibitin. Thus, these polypeptides
15 are expected to share biological activities with prohibitin. Such activities are known in
the art and discussed elsewhere herein.

This gene is expressed primarily in fetal brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a
20 biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, neural diseases. Similarly, polypeptides and antibodies directed to these
polypeptides are useful in providing immunological probes for differential identification
of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,
particularly of the nervous system, expression of this gene at significantly higher or
25 lower levels may be routinely detected in certain tissues and cell types (e.g., brain and
other tissue of the nervous system, and cancerous and wounded tissues) or bodily
fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or
cell sample taken from an individual having such a disorder, relative to the standard
gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an
30 individual not having the disorder. Preferred epitopes include those comprising a
sequence shown in SEQ ID NO. 153 as residues: Ala-85 to Ser-91, Pro-93 to Asp-98,
Glu-167 to Lys-173, Gln-205 to Ala-210.

The tissue distribution and structural similarity to prohibitin indicates that the protein products of this gene are useful for the detection/treatment of neurodegenerative
35 disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's
Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive
compulsive disorder, panic disorder, and autism. In addition, the gene or gene product

may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, and/or disorders of the cardiovascular system.

5 FEATURES OF PROTEIN ENCODED BY GENE NO: 44

The translation product of this gene shares sequence homology with the F44G4.1 gene of the *c. elegans* genome which has no known function (See Accession No.gnllPIDle236516). The translation product of this gene also shares sequence homology with the human torsionA and torsionB gene products, a gene candidate for the Torsion Dystonia disease locus (See Accession Nos gil2358279 (AF007871) and gil2358281 (AF007872)). One embodiment for this gene is the polypeptide fragments comprising the following amino acid sequence: KALALSFHGWSGTGKNFV (SEQ ID NO:284); NLIDYFIPFLPLEYRHVRLCAR (SEQ ID NO:285); NLIDYFIPFLPLEYRHVRLC (SEQ ID NO:286); CHQTLFIFDEAEKLHPGLLEVLGPHL (SEQ ID NO:287); and/or PEKALALSFHGWSGTGKNFVA (SEQ ID NO:288). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments.

This gene is expressed primarily in tonsils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, such as tonsillitis or adnoiditis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., tonsils, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution and homology to F44G4.1 gene of the *c. elegans* genome indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and detection of conditions affecting the tonsils. The tonsils have not been thoroughly studied and the actual function of this organ is not known, but this gene could be used in determining what may trigger tonsillitis. Especially in children, where the tonsils seem to be most active. Furthermore, due to the homology

of this gene, it may display potential utility in the detection, diagnosis, and/or treatment for Torsion Dystonia disease.

FEATURES OF PROTEIN ENCODED BY GENE NO: 45

- 5 Has exact sequence homology on the nucleotide level as Human HepG2 3' region cDNA, but the function of this gene is not known.

 This gene is expressed primarily in osteoclastoma stromal cells and to a lesser extent in T-cells.

- Therefore, polynucleotides and polypeptides of the invention are useful as
10 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, leukemia and bone disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of
15 the above tissues or cells, particularly of the haemolymphoid system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., bone tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene
20 expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of diseases such as leukemia.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 46

 This gene is expressed primarily in activated monocytes.

- Therefore, polynucleotides and polypeptides of the invention are useful as
30 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, including leukemia and allergies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the lymphoid system,
35 expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., hemopoietic cells, bone marrow, and spleen, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial

fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 156 as residues:

5 Met-1 to Gly-7.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment in tissue repair and modeling since monocytes engage the synthesis and secretion of many cytokines which are soluble proteins that regulate highly diverse aspects of cellular biology. Monocytes are also important in the fact that their expression of Major Histocompatibility Factor II (MHCII) enable them to select and stimulate the appropriate lymphocytes to combat specific antigens in the blood. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia.

FEATURES OF PROTEIN ENCODED BY GENE NO: 47

Translation product of this gene has homology to the Na⁺/H⁺-exchanging protein: Na⁺/H⁺ antiporter in *Methanobacterium thermoautotrophicum* as well as the Na⁺/H⁺ antiporter *cdu2'* in *Clostridium difficile* (See Accession Nos. gi12621849 (AE000854) and pir1JC5343/JC5343, respectively). Thus, it is likely that this gene has similar Na⁺/H⁺ antiporter activity. One embodiment for this gene are polypeptide fragments comprising the following amino acid sequence:

20 NLKEKIFISFAWLPKATVQAAIG (SEQ ID NO:289) and/or
25 WLPKATVQAAIGSVALD (SEQ ID NO:290). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments.

This gene is expressed primarily in osteoclastoma cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, osteoporosis, leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the lymphoid and skeletal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., bone cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell

sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 157 as residues: His-35 to Gln-43.

5 The tissue distribution predominantly in osteoclastoma cells (the site of hematopoiesis) indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of bone related diseases including osteoporosis, osteopetrosis and leukemia. Furthermore, its homology to known transporter proteins may suggest the protein is useful in the diagnosis, treatment, and
10 prevention of various developmental and metabolic disorders, particularly those based upon ion and proton transport.

FEATURES OF PROTEIN ENCODED BY GENE NO: 48

15 This gene is expressed primarily in amygdala and to a lesser extent in amniotic cells.

 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, depression and other emotional behavioral problems. Similarly,
20 polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., brain and tissues of the nervous system, and
25 tissues of the reproductive system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid or amniotic fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

30 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of mental problems associated with emotional behavior and neurodegenerative states such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorders, and
35 depression. The amygdala processes sensory information and relays this to other areas of the brain including the endocrine and autonomic domains of the hypothalamus and the brain stem. In addition, expression of this protein in amniotic cells suggests that

this protein would be useful in the diagnosis, prevention, and/or treatment of various developmental and/or reproductive system disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 49

- 5 This gene is expressed primarily in stromal cells.
- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, leukemia and other cancers and disorders deriving from hematopoietic
- 10 cells. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the lymphoid system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., haematopoietic tissues, and
- 15 cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or lymph fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.
- 20 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow
- 25 transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc.

30 FEATURES OF PROTEIN ENCODED BY GENE NO: 50

 This gene maps to chromosome 9, and therefore, may be used as a marker in linkage analysis for chromosome 9.

 This gene is expressed primarily in tumors, particularly skin and adrenal gland tumors, and to a lesser extent in bone marrow stromal cells and activated T cells.

- 35 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, cancer; hematopoietic and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, adrenal gland, and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endocrine glands, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 160 as residues: Glu-13 to Arg-22, Ser-58 to Trp-63.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of cancer. Elevated levels of expression of this gene in a variety of tumors suggest that it may play a role in cell proliferation, the induction of angiogenesis, destruction of the basal lamina, or a variety of other physiological processes that support the growth and development of tumors and cancer. Alternatively, its expression in the hematopoietic compartment, particularly in the bone marrow stroma and by activated T cells suggest that it may represent a soluble factor capable of influencing a variety of hematopoietic lineages. Therefore, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of blood cells.

25 FEATURES OF PROTEIN ENCODED BY GENE NO: 51

This gene is expressed primarily in benign human breast tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, breast cancer and other female reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the breast and reproductive tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., breast tissue, secretory/ductile organs, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid or milk) or another tissue or cell

sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides
5 corresponding to this gene are useful for the treatment and/or diagnosis of breast cancer. Alternately, this protein may play an important role in lactation or represent a critical component secreted into the milk, which may have an important function in the immunoprotection, health, and/or nourishment of the infant upon breastfeeding. Protein, as well as, antibodies directed against the protein may show utility as a tumor
10 marker and/or immunotherapy targets for the above listed tumors and tissues

FEATURES OF PROTEIN ENCODED BY GENE NO: 52

Translation product of this gene has homology with the conserved human ring
finger proteins (See Accession No.gnllPIDle351238 (AJ001019)) which are thought to
15 be important in facilitating and regulating signal transduction pathways in eukaryotic cells. One embodiment for this gene is the polypeptide fragments comprising the following amino acid sequence: HDRTMQDIVYKLV PGLQE (SEQ ID NO:291) and/or FASHDRTM QDIVYKLV PGLQEGE (SEQ ID NO:292). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments.

20 This gene is expressed primarily in adult whole brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative disorders; Schizophrenia; Alzheimer's; tumors of a
25 brain or neuronal cell origin. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the CNS and/or peripheral nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell
30 types (e.g., brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those
35 comprising a sequence shown in SEQ ID NO. 162 as residues: Phe-39 to Gly-44.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative

disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, considering the homology to the conserved ring finger proteins may suggest that the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo.

FEATURES OF PROTEIN ENCODED BY GENE NO: 53

- Translation product of this gene shares homology with the human conserved Lst-1 gene product, a member of the TNF family of proteins (See Accession No.gil1127546). One embodiment for this gene is the polypeptide fragments comprising the following amino acid sequence: LVLSLGAWGWPSTCLWW (SEQ ID NO:293). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments.
- This gene is expressed primarily in human 6-week old embryo.
- Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, abnormal cell proliferation; defects in terminal tissue differentiation.
- Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the embryo, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., proliferating and differentiating tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid or amniotic fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level; i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.
- The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or diagnosis of fetal disorders. Alternately, expression within embryonic tissues may reflect a role for this protein in proliferating cells. In such an event, this gene product may be useful in the treatment or diagnosis of abnormal cell proliferation, such as that involved in cancer.
- Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis involved in pattern formation. Thus, this protein may also be involved in apoptosis or tissue differentiation, and could again be useful in cancer therapy.

FEATURES OF PROTEIN ENCODED BY GENE NO: 54

This gene is expressed primarily in human epithelioid sarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as
5 reagents for differential identification of the tissue(s) or cell type(s) present in a
biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, epithelial sarcoma; tumors of an epithelial cell origin including the
underlying integument. Similarly, polypeptides and antibodies directed to these
polypeptides are useful in providing immunological probes for differential identification
10 of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,
particularly of the skin and epithelial tissue layers, expression of this gene at
significantly higher or lower levels may be routinely detected in certain tissues and cell
types (e.g., epithelial cells and tissue, and cancerous and wounded tissues) or bodily
fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or
15 cell sample taken from an individual having such a disorder, relative to the standard
gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an
individual not having the disorder. Preferred epitopes include those comprising a
sequence shown in SEQ ID NO. 164 as residues: Met-1 to Tyr-6, Thr-24 to Cys-36.

The tissue distribution indicates that polynucleotides and polypeptides
20 corresponding to this gene are useful for the treatment and/or diagnosis of epithelial
cancer. This gene product displays enhanced expression in epithelial cell sarcoma, and
thus may be involved in cell proliferation, apoptosis, or in the control of angiogenesis.

FEATURES OF PROTEIN ENCODED BY GENE NO: 55

25 This gene is expressed primarily in endometrial tumors.

Therefore, polynucleotides and polypeptides of the invention are useful as
reagents for differential identification of the tissue(s) or cell type(s) present in a
biological sample and for diagnosis of diseases and conditions which include, but are
not limited to, endometrial cancer including other cancers of the female reproductive
30 system. Similarly, polypeptides and antibodies directed to these polypeptides are useful
in providing immunological probes for differential identification of the tissue(s) or cell
type(s). For a number of disorders of the above tissues or cells, particularly of the
endometrium and reproductive system, expression of this gene at significantly higher or
lower levels may be routinely detected in certain tissues and cell types (e.g.,
35 endometrial tissue as well as other tissues of the female reproductive system, and
cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial
fluid or spinal fluid) or another tissue or cell sample taken from an individual having

such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of cancers, particularly those of the endometrium and other reproductive organs. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues

FEATURES OF PROTEIN ENCODED BY GENE NO: 56

This gene is expressed primarily in metastatic melanoma and to a lesser extent in fetal lung.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer of the integument system, particularly melanoma, as well as within the developing pulmonary system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., cells capable of forming melanin, epithelia, and lung, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or pulmonary surfactant) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 166 as residues: Asp-20 to Lys-25.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of cancer, particularly melanoma and more particularly, metastasizing melanomas. In addition, the tissue distribution also indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders. Expression in embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation or cellular division.

FEATURES OF PROTEIN ENCODED BY GENE NO: 57

This gene is expressed primarily in T-cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, lymphomas and other immune derived cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., T-cells and other cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 167 as residues: Met-1 to Asn-7.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of lymphomas, particularly T cell lymphomas, and other cancers. In addition, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders. Additionally, the expression in hematopoietic cells and tissues indicates that this protein may play a role in the proliferation, differentiation, and/or survival of hematopoietic cell lineages. Thus, this gene may be useful in the treatment of lymphoproliferative disorders, and in the maintenance and differentiation of various hematopoietic lineages from early hematopoietic stem and committed progenitor cells.

FEATURES OF PROTEIN ENCODED BY GENE NO: 58

This gene maps to chromosome 7, and therefore is useful in linkage analysis as a marker for chromosome 7.

This gene is expressed primarily in brain and to a lesser extent in spinal cord.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, CNS and PNS diseases and disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., brain, spinal cord and other tissue of the nervous system, and
5 cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 168 as residues:
10 Tyr-14 to Ala-30.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive
15 compulsive disorder, panic disorder, and autism.

FEATURES OF PROTEIN ENCODED BY GENE NO: 59

Translation product of this gene shares homology to the conserved *C. elegans* protein FER-1 (See Accession No.gil1373333). One embodiment for this gene is the
20 polypeptide fragments comprising the following amino acid sequence:
QGKLQMWVDVFPKSL (SEQ ID NO:294); PPFNITPRKAKKYLLR (SEQ ID NO:295); KTDVHYRSLDGEGNFNWRP (SEQ ID NO:296); and/or
PRLIIQIWDNDKFSLLDY LGFLELDL (SEQ ID NO:297). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments.

25 This gene is expressed primarily in synovial fibroblasts and to a lesser extent in synovial hypoxia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are
30 not limited to, synovial inflammation and other diseases of the joints. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the synovium, expression of this gene at significantly higher or lower levels may be routinely detected
35 in certain tissues and cell types (e.g., synovial tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to

the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases affecting the synovium of the joints, such as rheumatoid arthritis, osteoarthritis, other inflammatory conditions affecting the joints, as well as in the detection and treatment of disorders and conditions affecting the skeletal system, in particular the connective tissues (e.g. trauma, tendonitis, chondromalacia and inflammation). Furthermore, the homology to a conserved *C.elegans* protein may suggest protein is important in human development and thus is beneficial in the diagnosis, prevention, and treatment of developmental disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 60

This gene is expressed primarily in endothelial cells and to a lesser extent in brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation and other disorders of the integument, in addition to neurodegenerative and nervous system disorder, such as stroke. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endothelial, circulatory, and nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endothelial cells, and brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 170 as residues: Ser-4 to Gly-13.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of inflammatory diseases primarily mediated through endothelial cells, such as sepsis, inflammatory bowel disease, psoriasis, and Crohn's disease, as well as for stroke. Alternatively, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and

behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or disorders of the cardiovascular system.

FEATURES OF PROTEIN ENCODED BY GENE NO: 61

This gene is expressed primarily in fetal brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, CNS and PNS disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., developing and differentiating tissues, brain and other tissue of the nervous system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or amniotic fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of neural disorders such as Alzheimer's disease, depression, paranoia, schizophrenia, autism, and particularly developmental brain disorders..

FEATURES OF PROTEIN ENCODED BY GENE NO: 62

Translation product of this gene shares homology with a conserved 4-nitrophenylphosphatase from *Schizosaccharomyces pombe* (See Accession No. gil1938421). One embodiment for this gene is the polypeptide fragments comprising the following amino acid sequence: AVMIGDDCRDDVGGA (SEQ ID NO:298), and/or ILVKTGKYRASDEEKIN (SEQ ID NO:299). An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments. This gene maps to chromosome 18, and therefore, may be used as a marker in linkage analysis for chromosome 18.

This gene is expressed primarily in endometrial tumors and to a lesser extent in leukemia and lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer, particularly of the immune and hematopoietic systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endometrium and white blood cells, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endometrial and/or proliferating tissues, and cells and tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 172 as residues: Val-19 to Cys-24.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for detection, diagnosis, and treatment of cancers, particularly those cancers affecting endometrial tissues and the lymphatic system. In addition, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. Furthermore, homology to a conserved *S.pombe* protein may suggest protein is important in development. Therefore, protein may be beneficial in the diagnosis, prevention, and treatment of developmental disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 63

The translation product of this gene shares sequence homology with ribosomal releasing factor which is thought to be important in protein synthesis.

This gene is expressed primarily in pancreatic tumors, placenta, testis, ovarian cancer, adipocytes, spleen, and fetal liver and heart.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for diagnosis of a number of diseases and conditions such as immune-
5 diseases, cardiovascular and endocrine diseases and others. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, cardiovascular system, digestive system and reproductive system, expression of this
10 gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., pancreas, testis and ovary and other reproductive tissue, adipocytes, spleen, liver, and heart, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the
15 standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 173 as residues: Glu-36 to His-41, Thr-57 to Thr-70, Glu-87 to Met-92, Lys-100 to Lys-105, Ala-197 to Ser-227.

The tissue distribution and homology to ribosomal releasing factor indicates that
20 polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of many diseases, especially cancers and immuno-related diseases.

FEATURES OF PROTEIN ENCODED BY GENE NO: 64

The translation product of this gene shares sequence homology with
25 metalloprotease and also with thrombospondin, which is thought to be important in the activation of proteins and the processes of thrombopoiesis and metabolism.

This gene is expressed in many tissues, but especially in bladder, kidney, and ovary.

Therefore, polynucleotides and polypeptides of the invention are useful as
30 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of thrombopenia, hypertension, and other blood disfunctions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of
35 the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., urogenital, and reproductive tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma,

urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID

5 NO. 174 as residues: Gly-8 to Leu-14, Met-18 to Phe-30.

The tissue distribution and homology to thrombospondin indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of a variety of blood-related diseases.

10 **FEATURES OF PROTEIN ENCODED BY GENE NO: 65**

This gene is expressed primarily in tonsil, placenta, and fetal tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of many diseases of the immune system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., immune and developmental tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or amniotic fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases of the immune system including many cancers such as lymphomas, leukemias, lymphocytomas, and the like.

FEATURES OF PROTEIN ENCODED BY GENE NO: 66

30 Polypeptides encoded by this gene share reasonable homology to steroid/thyroid hormone orphan nuclear receptor and to several additional orphan nuclear receptors isolated from several different tissues.

This gene is expressed primarily in testis.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of testicular tumors, impotence, and other reproductive disorders. Similarly, polypeptides and antibodies directed to these

polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., male reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or seminal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- 10 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of diseases in the male reproductive system such as tumors of the testis and other reproductive disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 67

- 15 Polypeptides encoded by polynucleotides comprising this gene have a high degree of sequence identity with CTGF-4.

In one embodiment, the polypeptides of the invention comprise the sequence: MDSMPEPASRCLLLLPLLLLLLLLLPAPELGPSQAGAEENDWVRLPSK
CEVCKYVAVELKVKPLRKRQDTEVIGTVYGILDQKASGVKYTKSDLRLIEVTET
20 ICKRLLDYSLHKERTGSXRFAKGMSETFETLHXLVHKGVKVVM DIPYELWNE
TSAEVADLKKQCDVLVEEFEEVIEDWYRNHQEEDLTEFLCANHVLKKGKDTSC
AEQWSGKKGDTAALGGKSKKKSIRAKAAGGRSSSSKQRKELGGLEGDPSP
EEDEGIQKASPLTHSPPEL(SEQ ID NO:300). Polynucleotides encoding these
polypeptide sequences are also encompassed by the invention.

- 25 This gene is expressed in many tissues especially including cells in the immune system.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for the diagnosis of cancers, immunological disorders, and neural diseases (such as spinocerebellar ataxia, bipolar affective disorder, schizophrenia, and autism), and other diseases featuring anticipation, neurodegeneration, or abnormalities of neurodevelopment. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,
30 particularly of the nerve system, immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., immune cells and/or tissue, and cancerous and wounded tissues) or bodily

fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 177 as residues: Ser-3 to Ser-9, Gly-36 to Val-43, Leu-45 to Gly-51.

FEATURES OF PROTEIN ENCODED BY GENE NO: 68

Polypeptides encoded by polynucleotides comprising this gene contain a zinc finger homology domain. Such motifs are believed to be important for protein interactions, particularly with regard to gene regulation.

This gene is expressed primarily in T cells and the colon and, to a lesser extent, in the testes and placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of many immune and digestive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and digestive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., immune, gastrointestinal, and reproductive system tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, or seminal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 178 as residues: Pro-12 to Lys-33, Asn-41 to His-46, Pro-48 to Ser-58, Gly-71 to Asp-78, Ala-94 to Gly-102, Ser-133 to Ser-140, Arg-197 to Lys-202.

The expression of this gene in T-cells indicates a potential role in the treatment and detection of immune disorders such as arthritis, asthma, immune deficiency diseases (such as AIDS), and leukemia. Expression of this gene in the colon indicates a potential role in the treatment and detection of colon disorders such as ulcers and colon cancer in addition to digestive disorders in general.

FEATURES OF PROTEIN ENCODED BY GENE NO: 69

The translation product of this gene shares sequence homology with neuroendocrine protein, which is thought to be important in neuronal development and differentiation. A preferred embodiment of this gene comprises the following amino acid sequence: MDGQKKNWKDKVVDLLYWRDIKKTGVVFGASLFLLSLTVF
 5 SIVSVTAYIALALLSVTISFRIYKGVIAIQKSDEGHPFRAYLESEVAISEELVQKY
 SNSALGHVNCTIKELRRLFLVDDLVDLKFVLMWVFTYVGALFNLTLILAL
 ISLFSVPVIYERHQAQIDHYLGLANKNVKDAMAKIQAKIPGLKRKAE (SEQ ID
 10 NO:301). Particularly preferred are polynucleotides comprising polynucleotides encoding this polypeptide sequence.

This gene is expressed in many different tissues, but primarily in brain, and, to a lesser extent, in fetal tissue, placenta, bone marrow, and stromal cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for diagnosis of neurodegenerative diseases and developmental disorders.
 15 Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system and during development, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., neural,
 20 developmental, and hemopoietic cells and tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those
 25 comprising a sequence shown in SEQ ID NO. 179 as residues: Gln-47 to Gly-52, Leu-169 to Glu-174.

The predominant tissue distribution in brain and homology to neuroendocrine protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of neurodegenerative diseases and behavioral
 30 disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive-compulsive disorder and panic disorder.

FEATURES OF PROTEIN ENCODED BY GENE NO: 70

35 Polypeptides encoded by polynucleotides comprising this gene share sequence identity with human hepatoma-derived growth factor (WPI 95-069304/10). As such, polynucleotides comprising this gene can be used for the recombinant production of the

protein, which can be used to encourage the growth of various animal cells, and for the purification of receptors. Additional embodiments of the invention comprise the following polypeptide sequences: MAVTLSLLLGGRVCA (SEQ ID NO:302); PSLAVGSRPGGW RAQALLAGSRTPIPTGSRNGSCRRWRAP (SEQ ID NO:303); and/or MAVTLSLLLGGRVCAPSLAVGSRPGGWRAQALLAGSRTPIPTG

5 SRRNGSCRRWRAP (SEQ ID NO:304). Also contemplated are polynucleotides comprising polynucleotides encoding the aforementioned polypeptide sequences.

This gene is expressed primarily in brain and to a lesser extent in endothelium, T- cell, and tumors.

10 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of many neurodegenerative diseases (for example, Alzheimer's Disease, ALS, and the like) and cancers (including, but not limited to neuroblastoma, glioblastoma, Schwannoma, astrocytoma, and the like). Similarly,

15 polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., neural, and haematopoietic cells and tissue, and

20 cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid or lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID

25 NO. 180 as residues: Pro-4 to Thr-10, Glu-25 to Trp-30, Leu-58 to Leu-69, Arg-82 to Thr-87, Ala-108 to His-115, Ser-124 to Glu-146, Pro-159 to Gly-176, Ser-182 to Glu-187, Leu-189 to Ser-198, Phe-208 to Asn-214.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of many

30 neurodegenerative diseases and cancers.

FEATURES OF PROTEIN ENCODED BY GENE NO: 71

The translation product of this gene shares sequence homology with acrosin, trypsin, as well as trypsinogen precursor which are thought to be important in cell-cell

35 recognition and proteinase activity for protein cleavage and degradation. Preferred polynucleotide fragments comprise the following sequence:

GATGTTACACAGCTCTTTAATAATAGTGGCCATAGCTGTAATAACAATGACA

ACAGTAGGTAACGGTAGTCATACCAACAGTAGGGCAGTGCATTTTATATTAC
 AACTGGTTTCTTGCTCTAGTAGGCTTGGGGATGGGTGAAGACGGACAGGGC
 TGGCGCAGACCCTTTCCTTCTCCTCTCCAGCCACAGTCTCTGGGCTTTTA
 CAGACAGCCTGCTTCCATTCACTAGTGTGGGAAAGTCTTCTTGCTTAGC
 5 AATACCCCTGAGACCTTGTTCACTGGGCTGTGTCTCTCCCTGGGATGCTGG
 GAGACCAAGTGTGGCCGAGCTAGGGCTGCTGACTTCCTCTGGGCGCCTCT
 GGGCTGCGAGGGTCTCTTATAGGAATTGAGGCCCTTTGCTGCTCCAAGAAA
 TGCGAGGCTGTGGGCARAGGGKTGTACCCAAGGGGACTCTTGCTCTGTGT
 CTGACTTTGGGGRATCC (SEQ ID NO:305); CACAGCTCTTTAATAATAGTGGC
 10 CATAGCTGTAATAACAATGACA ACAGTAGGTAACG (SEQ ID NO:306);
 TGTGTCTCTCCCTGGGATGCTGGGAGCACCAAGTGTGGCCGAGCTAGGGCT
 GCTGACTT (SEQ ID NO:307); GCGAGGGTCTCTTATAGGAATTGAGGCCCTT
 TGCTGCTCCAAGAAATGCTGAGGCTGTGGGCARAGGGKTGTACCCAAGGG
 GACT (SEQ ID NO:308). Also preferred are polypeptide fragments encoded by these
 15 polynucleotide fragments.

This gene is expressed primarily in cheek carcinoma and to a lesser extent in
 uterine and pancreatic cancers.

Therefore, polynucleotides and polypeptides of the invention are useful as
 reagents for differential identification of the tissue(s) or cell type(s) present in a
 20 biological sample and for diagnosis of diseases and conditions which include, but are
 not limited to, cheek cancers or cancers of uterine and pancreatic origins. Similarly,
 polypeptides and antibodies directed to these polypeptides are useful in providing
 immunological probes for differential identification of the tissue(s) or cell type(s). For a
 number of disorders of the above tissues or cells, particularly of the neoplastic tissues,
 25 expression of this gene at significantly higher or lower levels may be routinely detected
 in certain tissues and cell types (e.g., epithelial, endocrine, and reproductive tissues,
 and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine,
 synovial fluid, spinal fluid, and saliva) or another tissue or cell sample taken from an
 individual having such a disorder, relative to the standard gene expression level, i.e.,
 30 the expression level in healthy tissue or bodily fluid from an individual not having the
 disorder.

The tissue distribution and homology to acrosin and trypsin indicates that
 polynucleotides and polypeptides corresponding to this gene are useful for diagnosis
 and intervention of cancers. The homology to acrosin and trypsin may indicate the gene
 35 function in tumor metastasis or migration since in both cases cell-cell interaction and
 extracellular matrix degradation may be involved. The gene product can also be used as
 a target for cancer immunotherapy or as a diagnostic marker.

FEATURES OF PROTEIN ENCODED BY GENE NO: 72

This gene is expressed primarily in T helper cells I, T-cells stimulated with PHA for 24 hours, and in a placenta Nb2HP cDNA library.

5 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of many immunodeficiencies and disorders (especially autoimmune diseases). Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential
10 identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., immune, and haematopoietic cells and tissue, and cancerous and wounded tissue) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid and
15 lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of autoimmune
20 diseases, immunodeficiencies, and other immune system disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 73

This gene is expressed primarily in 7 week old early stage human, human chronic synovitis, and infant brain.

25 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of chronic synovitis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders
30 of the above tissues or cells, particularly of the synovium, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., developmental, differentiating, and neural tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, and amniotic fluid) or another tissue or cell sample taken from an individual
35 having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the

disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 183 as residues: Ser-44 to Pro-49.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of chronic synovitis and other disorders of the synovium.

FEATURES OF PROTEIN ENCODED BY GENE NO: 74

Polypeptides encoded by polynucleotides comprising this gene exhibit sequence homology to a number of mucin-like extracellular or cell surface proteins. In one embodiment polypeptides of the invention comprise the following sequence:
 MVGPVTLHKKIHTTTVLFIHQIHILLIQAITQAK (SEQ ID NO:309); LQMHLMLQ
 MTGLSILALLGKSTTTIVEQKFHNGKNQKSGLENRDKKKQTRWQSTASQKI
 GITEER (SEQ ID NO:310); and/or MVGPVTLHKKIHTTTVLFIHQIHILLIQAITQ
 AKLQMHLMLQMTGLSILALLGKSTTTIVEQKFHNGKNQKSGLENRDKKKQ
 TRWQSTASQKIGITEER (SEQ ID NO:311). Polynucleotides encoding the
 aforementioned polypeptides are also contemplated embodiments of the invention.

This gene is expressed primarily in ovarian cancer, endometrial tumor, B-cell lymphoma, brain-medulloblastoma, hepatocellular tumor, osteosarcoma, and T- and B-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, Ovarian cancer, endometrial tumor, B-cell lymphoma, brain medulloblastoma, hepatocellular tumor, and osteosarcoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., brain and other tissue of the nervous system, bone, T-cells and other cells of the immune system, and B cells and other blood cells, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid and lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 184 as residues: Met-1 to Lys-12, Leu-14 to Asn-35, Arg-42 to Asn-58, Ser-65 to Trp-90, Ser-95 to Asn-129, Phe-136 to Arg-144, Met-159 to Ala-167, Thr-179 to Tyr-187, Pro-190 to

Val-201, Gln-226 to Phe-235, Pro-254 to His-272, Thr-288 to Thr-293, Thr-383 to Ser-391, Asp-398 to Tyr-405, Ile-410 to Asn-416, Ala-449 to Lys-458.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of ovarian cancer, endometrial tumors, B-cell lymphoma, brain medulloblastoma, hepatocellular tumor, and osteosarcoma.

FEATURES OF PROTEIN ENCODED BY GENE NO: 75

An additional preferred polypeptide sequence derived from the polynucleotide of this contig comprises the following amino acid sequence: MQTCPLVGTLTRNMDG YTCAVVTSTSFWIISAWXLWKGSPSTSMPTMPETPLRTLCCCKMPSIFSSLMTD GRA (SEQ ID NO:312). Polynucleotides encoding these polypeptides are also provided. This polypeptide sequence has sequence homology with a *Drosophila melanogaster* male germ-line specific transcript which encodes a putative protamine molecule (see, gil608696).

This gene is expressed primarily in breast tissue and to a lesser extent in various other fetal and adult cells and tissues, especially those comprising endocrine organs.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and reproductive defects. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the female reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., breast and/or other ductile secretory tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, and milk) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of developmental, reproductive and growth and metabolic disorders.

35 FEATURES OF PROTEIN ENCODED BY GENE NO: 76

In one embodiment, the polypeptides of the invention comprise the sequence: MTLIQNCWYSWLFFGFFFHFLRKSISIFSIFLVCFRILALGPTCFLVFWFKAFFR

HILIFICLSREVFPRCFLVYFR (SEQ ID NO:313). This polypeptide sequence has sequence homology with the MURF4 protein of *Herpetomonas muscarum* (S43288). Such RNA-editing enzymes may be useful as molecular targets in the intervention of the life cycle of trypanosomes and other protozoa. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in fetal liver and spleen, osteosarcoma and bone marrow.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of liver tumors, osteosarcoma, and other cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., hepatic, developmental, and differentiating tissue, bone cells, liver and spleen, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, and lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis of cancers such as liver tumor and osteosarcoma.

25 FEATURES OF PROTEIN ENCODED BY GENE NO: 77

This gene is expressed primarily in T cell lymphoma and monocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of T-cell lymphoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., immune and hematopoietic cells and tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, and lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in

healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 187 as residues: Thr-1 to Ser-9.

The tissue distribution indicates that polynucleotides and polypeptides
5 corresponding to this gene are useful for diagnosis and treatment of T-cell lymphoma.

FEATURES OF PROTEIN ENCODED BY GENE NO: 78

This gene is expressed primarily in tonsils and a bone marrow cell line.

Therefore, polynucleotides and polypeptides of the invention are useful as
10 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of immunological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system,
15 expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., haematopoietic and immune cells and tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, and lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the
20 expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides
corresponding to this gene are useful for the diagnosis and treatment of immunological disorders.

25

FEATURES OF PROTEIN ENCODED BY GENE NO: 79

In one embodiment, the polypeptides of the invention comprise the sequence:
MGTRAQVTPGRLPIPPAPGLPFSAXEPLQGQLRRVSSSRGGFPGLALQLLRSE
TVKAYVNNEINILASFF (SEQ ID NO:314) and/or MLVRTRPSQLPLPGVGLGGP
30 RSGDPPESTELRKGPGLA (SEQ ID NO:315). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in brain, placenta, bone marrow, keratinocyte, fetal liver, and spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as
35 reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of brain and skin related diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing

immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and skin system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., neural, reproductive, and hepatic tissues, 5 keratinocytes, and spleen, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a 10 sequence shown in SEQ ID NO. 189 as residues: Phe-13 to Leu-18.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of many brain and skin related diseases.

15 **FEATURES OF PROTEIN ENCODED BY GENE NO: 80**

The translation product of this gene shares sequence homology with mouse RNA Polymerase I which is thought to be important in gene transcription process.

This gene is expressed primarily in HEL cell line and aorta endothelial cells and to a lesser extent in Jurkat T-cells.

20 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis and treatment of cancer and autoimmune diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell 25 type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endothelial, haematopoietic tissues, cardiovascular tissue, and T-cells and other cells of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial 30 fluid, spinal fluid, and lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 190 as residues: Lys-25 to Arg-32.

35 The tissue distribution and homology to mouse RNA polymerase I indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of immune diseases and cardiovascular diseases.

FEATURES OF PROTEIN ENCODED BY GENE NO: 81

In one embodiment, the polypeptides of the invention comprise the sequence:

MCPVCGRALSSPGSLGRHLLIHSEDQRSNCAVCGARFTSHATFNSEKLPEVLN
5 MESLPTVHNEGPPSSAEGKDIAFSPPVYPAGILLVCNNCAAYRKXLEAQTSPVX
KWALRRQNEPLEVRLQRLERERTAKKSRRDNETPEEREVRRMRDREAKRLQR
MQETDEQRARRLQRDREAMRLKRANETPEKRQARLIREREAKRLKRRLEKMD
MMLRAQFGQDPSAMAALAAEMNFFQLPVSGVELDXQLLGKMAFEEQNSSXLH
(SEQ ID NO:316). This polypeptide shares sequence homology with human trichohylin
10 which is thought to be important in gene regulation. Polynucleotides encoding this
polypeptide are also encompassed by the invention.

This gene is expressed primarily in brain tissue and to a lesser extent in apoptotic T-cell and B-cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as
15 reagents for differential identification of the tissue(s) or cell type(s) present in a
biological sample and for diagnosis and treatment of growth disorders,
neurodegenerative diseases, and endocrine disorders. Similarly, polypeptides and
antibodies directed to these polypeptides are useful in providing immunological probes
for differential identification of the tissue(s) or cell type(s). For a number of disorders
20 of the above tissues or cells, particularly of the neural and immune systems, expression
of this gene at significantly higher or lower levels may be routinely detected in certain
tissues and cell types (e.g., neural tissues, T-cells, B-cells and other cells and tissue of
the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum,
plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from
25 an individual having such a disorder, relative to the standard gene expression level, i.e.,
the expression level in healthy tissue or bodily fluid from an individual not having the
disorder.

The tissue distribution and homology to DNA binding protein indicates that
polynucleotides and polypeptides corresponding to this gene are useful for the
30 diagnosis and treatment of immune and neurological diseases.

FEATURES OF PROTEIN ENCODED BY GENE NO: 82

In one embodiment, the polypeptides of the invention comprise the sequence:

MDHSHHMGMSYMDSNSTMQPSHHPTTSASHSHGGDSSMMMMPMFTFYFG
35 FKNVELLFSGLVINTAGEMAGAFVAVFLAMFYEGLKIARESLLRKSQVSIRYN
SMPVPGPNGTILMETHKTVGQQMLSFPHLLQTVLHIIQVVISYFLMLIFMTYNG
YLCIAXAAGAGTGYFLFSWKKAVVVDITEHCH (SEQ ID NO:317). This

polypeptide is thought to function in mediating the uptake of copper and other metal ions by cells. Polynucleotides encoding this polypeptide are also encompassed by the invention.

5 This gene is expressed primarily in osteosarcoma and to a lesser extent in T-cell and bone marrow stromal cell.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for treatment and diagnosis of osteosarcoma and copper and other metal uptake disorders. Similarly, polypeptides and antibodies directed to these
10 polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., hematopoietic tissue and cancerous and wounded tissues) or bodily fluids (e.g.,
15 serum, plasma, urine, synovial fluid, spinal fluid, and lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 192 as residues: Ser-24 to Ser-29.

20 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the prevention or treatment of osteosarcoma and copper or other metal uptake disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 83

25 This gene is expressed primarily in skin tumor and to a lesser extent in apoptic T-cell.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are
30 not limited to, skin tumor. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., epithelial and
35 hematopoietic tissues, and T-cells and other tissue of the immune system, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, and spinal fluid) or another tissue or cell sample taken from an individual having

such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 193 as residues: Leu-51 to Gly-77, Ile-117 to Pro-125.

- 5 The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis the treatment of skin tumor.

FEATURES OF PROTEIN ENCODED BY GENE NO: 84

This gene is expressed primarily in testis.

- 10 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, infertility and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes
- 15 for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., reproductive tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, and seminal fluid) or
- 20 another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

- The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of reproductive disease and
- 25 endocrine disorders.

FEATURES OF PROTEIN ENCODED BY GENE NO: 85

In one embodiment, the polypeptides of the invention comprise the sequence:
 MVQPCGACAKTXWKACSSCCSSPCCLQERWPXPXAXCPEXGPSSHPGIQALC
 30 AVAVVYLSRSSRLDWSLAPLFVPSLAAGETPLTQPAWALTNTLGHGQPAQDR
 LPALGHCAISVLGLGSS (SEQ ID NO:318). Polynucleotides encoding this polypeptide sequence are also encompassed by the invention.

This gene is expressed primarily in kidney cortex, frontal cortex, spinal cord and hippocampus.

- 35 Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, kidney fibrosis, schizophrenia and neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neural system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., endothelial, neural and endocrine tissue, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid or spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 195 as residues: Cys-27 to Tyr-33, Thr-38 to Gly-43, Leu-125 to Gly-130.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of neurological disorders and kidney diseases.

FEATURES OF PROTEIN ENCODED BY GENE NO: 86

This gene is expressed primarily in resting T-cell.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, T-cell related diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues and cell types (e.g., hematopoietic and immune cells and tissues, and cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid, spinal fluid, and lymph) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, (i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder). Preferred epitopes include those comprising a sequence shown in SEQ ID NO. 196 as residues: Thr-54 to Ile-59.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of immune diseases.

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--|-----------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 1 | HOAAE80 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 11 | 1220 | 264 | 1220 | 288 | 288 | 111 | 1 | 26 | 27 | 31 |
| 2 | HODDN92 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 12 | 1939 | 294 | 1939 | 434 | 434 | 112 | 1 | 26 | 27 | 35 |
| 3 | HOSBI96 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 13 | 2602 | 672 | 1811 | 690 | 690 | 113 | 1 | 30 | 31 | 219 |
| 4 | HOVAI58 | 209012 04/28/97 209089 06/05/97 | pSport1 | 14 | 808 | 1 | 808 | 28 | 28 | 114 | 1 | 26 | 27 | 31 |
| 5 | HPBDD36 | 209012 04/28/97 209089 06/05/97 | pBluescript SK- | 15 | 864 | 87 | 831 | 147 | 147 | 115 | 1 | 18 | 19 | 26 |
| 6 | HPDDC77 | 209012 04/28/97 209089 06/05/97 | pBluescript SK- | 16 | 2361 | 455 | 1442 | 510 | 510 | 116 | 1 | 29 | 30 | 131 |
| 7 | HPEBD85 | 209012 | Uni-ZAP XR | 17 | 803 | 1 | 803 | 81 | 81 | 117 | 1 | 20 | 21 | 64 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--|-------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| | | 04/28/97 209089 06/05/97 | | | | | | | | | | | | |
| 8 | HPFCX38 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 18 | 1794 | 1051 | 1757 | | 578 | 118 | 1 | | | 8 |
| 9 | HPFCY51 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 19 | 1037 | 1 | 1037 | 467 | 467 | 119 | 1 | 30 | 31 | 50 |
| 9 | HPFCY51 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 97 | 1052 | 1 | 1052 | 30 | 30 | 197 | 1 | | | 13 |
| 10 | HPMGQ80 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 20 | 1309 | 157 | 1309 | 360 | 360 | 120 | 1 | 19 | 20 | 76 |
| 11 | HPRTG55 | 209012 04/28/97 209089 06/05/97 | pBluescript | 21 | 1081 | 55 | 1014 | 237 | 237 | 121 | 1 | 24 | 25 | 26 |
| 12 | HROAN56 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 22 | 807 | 1 | 807 | 26 | 26 | 122 | 1 | 19 | 20 | 23 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--|-----------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 13 | HSAB142 | 209012 04/28/97 209089 06/05/97 | pBluescript SK- | 23 | 632 | 1 | 596 | 190 | 190 | 123 | 1 | 15 | 16 | 21 |
| 14 | HSAUW44 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 24 | 1358 | 1 | 1358 | 372 | 372 | 124 | 1 | 30 | 31 | 54 |
| 15 | HSDES04 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 25 | 1376 | 686 | 1376 | 146 | 146 | 125 | 1 | 33 | 34 | 318 |
| 15 | HSDES04 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 98 | 929 | 57 | 929 | 291 | 291 | 198 | 1 | 28 | 29 | 61 |
| 16 | HSHBQ68 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 26 | 2923 | 195 | 2642 | 211 | 211 | 126 | 1 | 23 | 24 | 58 |
| 17 | HSKBO20 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 27 | 775 | 1 | 501 | | 308 | 127 | 1 | 28 | 29 | 98 |
| 18 | HSKNM85 | 209012 04/28/97 209089 | pBluescript | 28 | 534 | 1 | 534 | 122 | 122 | 128 | 1 | 19 | 20 | 28 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--|-------------|-----------------|---------------|---------------------|---------------------|---------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 19 | HSKXJ37 | 209012 04/28/97 209089 06/05/97 | pBluescript | 29 | 1827 | 67 | 1634 | 311 | 129 | 1 | 21 | 22 | 21 |
| 20 | HSKZE52 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 30 | 1479 | 418 | 1453 | 555 | 130 | 1 | 18 | 19 | 111 |
| 21 | HWTZ75 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 31 | 987 | 448 | 963 | 133 | 131 | 1 | 1 | 2 | 114 |
| 22 | HSRBA90 | 209012 04/28/97 209089 06/05/97 | Uni-ZAP XR | 32 | 2933 | 1437 | 2933 | 1670 | 132 | 1 | 19 | 20 | 21 |
| 23 | HSVAG05 | 209090 06/05/97 | Uni-ZAP XR | 33 | 1366 | 1 | 1366 | 66 | 133 | 1 | 31 | 32 | 51 |
| 24 | HSVBF78 | 209090 06/05/97 | Uni-ZAP XR | 34 | 667 | 141 | 621 | 64 | 134 | 1 | 28 | 29 | 99 |
| 25 | HSXBO51 | 209090 06/05/97 | Uni-ZAP XR | 35 | 1710 | 388 | 1683 | 462 | 135 | 1 | 26 | 27 | 175 |
| 26 | HT3BE24 | 209090 06/05/97 | Uni-ZAP XR | 36 | 1096 | 756 | 1091 | 422 | 136 | 1 | 15 | 16 | 187 |
| 26 | HT3BE24 | 209090 06/05/97 | Uni-ZAP XR | 99 | 359 | 1 | 359 | 41 | 199 | 1 | 42 | 43 | 71 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--------------------------|------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 27 | HT4AI54 | 209090 06/05/97 | Uni-ZAP XR | 37 | 2279 | 1387 | 2279 | 29 | 29 | 137 | 1 | 24 | 25 | 288 |
| 27 | HT4AI54 | 209090 06/05/97 | Uni-ZAP XR | 100 | 952 | 1 | 952 | 199 | 199 | 200 | 1 | | | 10 |
| 28 | HTEHU93 | 209090 06/05/97 | Uni-ZAP XR | 38 | 745 | 1 | 745 | 187 | 187 | 138 | 1 | 24 | 25 | 113 |
| 29 | HTGCCQ82 | 209090 06/05/97 | Uni-ZAP XR | 39 | 1718 | 70 | 1718 | 114 | 114 | 139 | 1 | 23 | 24 | 119 |
| 30 | HTLAB25 | 209090 06/05/97 | Uni-ZAP XR | 40 | 1966 | 321 | 1966 | 449 | 449 | 140 | 1 | 1 | 2 | 438 |
| 31 | HTLAV68 | 209090 06/05/97 | Uni-ZAP XR | 41 | 972 | 1 | 972 | 78 | 78 | 141 | 1 | 35 | 36 | 162 |
| 32 | HTLDQ11 | 209090 06/05/97 | Uni-ZAP XR | 42 | 1536 | 1 | 1536 | 213 | 213 | 142 | 1 | 36 | 37 | 72 |
| 33 | HTOBX52 | 209090 06/05/97 | Uni-ZAP XR | 43 | 2541 | 1743 | 2541 | | 3 | 143 | 1 | 4 | 5 | 123 |
| 34 | HTTCN24 | 209090 06/05/97 | Uni-ZAP XR | 44 | 2418 | 918 | 2290 | 188 | 188 | 144 | 1 | 30 | 31 | 138 |
| 34 | HTTCN24 | 209090 06/05/97 | Uni-ZAP XR | 101 | 1545 | 123 | 1545 | 345 | 345 | 201 | 1 | 39 | 40 | 50 |
| 35 | HTXCS21 | 209090 06/05/97 | Uni-ZAP XR | 45 | 1337 | 657 | 1309 | 76 | 76 | 145 | 1 | 24 | 25 | 356 |
| 35 | HTXCS21 | 209090 06/05/97 | Uni-ZAP XR | 102 | 1322 | 641 | 1293 | | 1203 | 202 | 1 | | | 13 |
| 36 | HUFAC49 | 209090 06/05/97 | pSport1 | 46 | 1276 | 1 | 1276 | 105 | 105 | 146 | 1 | 17 | 18 | 39 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--------------------------|-----------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 37 | HAIDK60 | 209090 06/05/97 | Uni-ZAP XR | 47 | 1282 | 1 | 1282 | 528 | 528 | 147 | 1 | 30 | 31 | 71 |
| 37 | HAIDK60 | 209090 06/05/97 | Uni-ZAP XR | 103 | 276 | 1 | 276 | 14 | 14 | 203 | 1 | 25 | 26 | 38 |
| 38 | HARAG28 | 209090 06/05/97 | pBluescript SK- | 48 | 645 | 1 | 645 | 150 | 150 | 148 | 1 | 16 | 17 | 33 |
| 38 | HARAG28 | 209090 06/05/97 | pBluescript SK- | 104 | 381 | 1 | 381 | 154 | 154 | 204 | 1 | 18 | 19 | 34 |
| 39 | HMBB80 | 209090 06/05/97 | pBluescript | 49 | 1495 | 2 | 1495 | 23 | 23 | 149 | 1 | 30 | 31 | 78 |
| 39 | HMBB80 | 209090 06/05/97 | pBluescript | 105 | 638 | 1 | 638 | 196 | 196 | 205 | 1 | 16 | 17 | 26 |
| 40 | HCEGR33 | 209090 06/05/97 | Uni-ZAP XR | 50 | 1630 | 1 | 1630 | 243 | 243 | 150 | 1 | 22 | 23 | 31 |
| 41 | HSXBP68 | 209090 06/05/97 | Uni-ZAP XR | 51 | 2420 | 1009 | 2252 | 79 | 79 | 151 | 1 | 41 | 42 | 464 |
| 41 | HSXBP68 | 209090 06/05/97 | Uni-ZAP XR | 106 | 2246 | 835 | 2079 | 985 | 985 | 206 | 1 | 32 | 33 | 105 |
| 42 | HFFAT33 | 209090 06/05/97 | Lambda ZAP II | 52 | 1172 | 166 | 802 | 209 | 209 | 152 | 1 | 29 | 30 | 151 |
| 43 | HFGAG96 | 209090 06/05/97 | Uni-ZAP XR | 53 | 1589 | 885 | 1446 | 189 | 189 | 153 | 1 | 33 | 34 | 299 |
| 43 | HFGAG96 | 209090 06/05/97 | Uni-ZAP XR | 107 | 1105 | 1 | 1105 | | | 207 | 1 | 17 | 18 | 64 |
| 44 | HETFI05 | 209076 05/22/97 | Uni-ZAP XR | 54 | 2074 | 1 | 2065 | 75 | 75 | 154 | 1 | 24 | 25 | 397 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--------------------------|-------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 45 | HLTEY63 | 209076 05/22/97 | Uni-ZAP XR | 55 | 1483 | 1 | 1280 | 86 | 86 | 155 | 1 | 18 | 19 | 82 |
| 46 | HMSJU68 | 209076 05/22/97 | Uni-ZAP XR | 56 | 1123 | 4 | 1123 | 272 | 272 | 156 | 1 | 31 | 32 | 49 |
| 47 | HOSCZ41 | 209076 05/22/97 | Uni-ZAP XR | 57 | 1239 | 117 | 1222 | 178 | 178 | 157 | 1 | 20 | 21 | 50 |
| 48 | HSHAV28 | 209076 05/22/97 | Uni-ZAP XR | 58 | 803 | 105 | 719 | | 378 | 158 | 1 | | | 16 |
| 49 | HSQEA85 | 209076 05/22/97 | Uni-ZAP XR | 59 | 995 | 1 | 995 | 98 | 98 | 159 | 1 | 23 | 24 | 52 |
| 50 | HSTAG52 | 209076 05/22/97 | Uni-ZAP XR | 60 | 966 | 114 | 966 | 191 | 191 | 160 | 1 | 45 | 46 | 63 |
| 51 | HBNAJ22 | 209076 05/22/97 | Uni-ZAP XR | 61 | 262 | 1 | 262 | 28 | 28 | 161 | 1 | 23 | 24 | 32 |
| 52 | HBXGP76 | 209076 05/22/97 | ZAP Express | 62 | 753 | 1 | 753 | 34 | 34 | 162 | 1 | 34 | 35 | 94 |
| 53 | HE6GL64 | 209076 05/22/97 | Uni-ZAP XR | 63 | 739 | 1 | 739 | 132 | 132 | 163 | 1 | 32 | 33 | 57 |
| 54 | HESAL35 | 209076 05/22/97 | Uni-ZAP XR | 64 | 476 | 1 | 476 | 20 | 20 | 164 | 1 | 27 | 28 | 43 |
| 55 | HETBB70 | 209076 05/22/97 | Uni-ZAP XR | 65 | 754 | 14 | 754 | | 263 | 165 | 1 | 17 | 18 | 17 |
| 56 | HLHAY19 | 209076 05/22/97 | Uni-ZAP XR | 66 | 1890 | 8 | 1890 | 18 | 18 | 166 | 1 | 22 | 23 | 28 |
| 57 | HLTER45 | 209076 05/22/97 | Uni-ZAP XR | 67 | 1614 | 557 | 1614 | 578 | 578 | 167 | 1 | 25 | 26 | 36 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--------------------------|-----------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 58 | HNHAL34 | 209076 05/22/97 | Uni-ZAP XR | 68 | 596 | 1 | 596 | 90 | 90 | 168 | 1 | 18 | 19 | 39 |
| 59 | HOSFF78 | 209076 05/22/97 | Uni-ZAP XR | 69 | 1524 | 791 | 1524 | 846 | 846 | 169 | 1 | 34 | 35 | 46 |
| 60 | HSKDV92 | 209076 05/22/97 | Uni-ZAP XR | 70 | 819 | 53 | 819 | | 158 | 170 | 1 | 32 | 33 | 33 |
| 61 | HFCCU63 | 209076 05/22/97 | Uni-ZAP XR | 71 | 1442 | 1 | 1442 | 12 | 12 | 171 | 1 | | | 4 |
| 62 | HLTCS34 | 209076 05/22/97 | Uni-ZAP XR | 72 | 1223 | 1 | 1223 | 227 | 227 | 172 | 1 | 17 | 18 | 24 |
| 63 | HPMCC16 | 209086 05/29/97 | Uni-ZAP XR | 73 | 1814 | 1024 | 1814 | 85 | 85 | 173 | 1 | 19 | 20 | 262 |
| 64 | HOUQC17 | 209086 05/29/97 | Uni-ZAP XR | 74 | 4712 | 1 | 4693 | 508 | 508 | 174 | 1 | 51 | 52 | 967 |
| 65 | HTDAG66 | 209086 05/29/97 | pSport1 | 75 | 1885 | 262 | 1885 | 369 | 369 | 175 | 1 | | | 18 |
| 66 | HTLBC79 | 209086 05/29/97 | Uni-ZAP XR | 76 | 890 | 1 | 890 | 17 | 17 | 176 | 1 | 1 | 2 | 205 |
| 67 | HTOFC34 | 209086 05/29/97 | Uni-ZAP XR | 77 | 1657 | 356 | 1645 | 434 | 434 | 177 | 1 | 31 | 32 | 54 |
| 68 | H2CBJ08 | 209086 05/29/97 | pBluescript SK- | 78 | 2015 | 13 | 2015 | 70 | 70 | 178 | 1 | 17 | 18 | 435 |
| 69 | HAGFT48 | 209086 05/29/97 | Uni-ZAP XR | 79 | 1213 | 242 | 1213 | | 290 | 179 | 1 | 23 | 24 | 174 |
| 70 | HCE5M29 | 209086 05/29/97 | Uni-ZAP XR | 80 | 1391 | 23 | 1353 | 251 | 251 | 180 | 1 | 1 | 2 | 219 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--------------------------|---------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 71 | HTPBQ83 | 209076 05/22/97 | Uni-ZAP XR | 81 | 1008 | 146 | 1008 | | 431 | 181 | 1 | | | 5 |
| 72 | HCFNN01 | 209086 05/29/97 | pSport1 | 82 | 1261 | 154 | 1261 | 254 | 254 | 182 | 1 | 27 | 28 | 43 |
| 73 | HE7TF86 | 209086 05/29/97 | Uni-ZAP XR | 83 | 1045 | 241 | 986 | 426 | 426 | 183 | 1 | 23 | 24 | 58 |
| 74 | HGBAC11 | 209086 05/29/97 | Uni-ZAP XR | 84 | 2877 | 1 | 2272 | 85 | 85 | 184 | 1 | 1 | 2 | 588 |
| 75 | HHGAU81 | 209086 05/29/97 | Lambda ZAP II | 85 | 1367 | 747 | 1367 | 323 | 323 | 185 | 1 | 24 | 25 | 166 |
| 76 | HLCAA05 | 209086 05/29/97 | Uni-ZAP XR | 86 | 1009 | 1 | 1009 | 276 | 276 | 186 | 1 | | | 8 |
| 77 | HMSCD68 | 209086 05/29/97 | Uni-ZAP XR | 87 | 1367 | 1 | 1367 | | 254 | 187 | 1 | | | 12 |
| 78 | HMWDD81 | 209086 05/29/97 | Uni-Zap XR | 88 | 1088 | 1 | 883 | 214 | 214 | 188 | 1 | 22 | 23 | 30 |
| 79 | HMWGGQ73 | 209086 05/29/97 | Uni-Zap XR | 89 | 1861 | 875 | 1861 | | 1160 | 189 | 1 | 15 | 16 | 18 |
| 80 | HOECN31 | 209086 05/29/97 | Uni-ZAP XR | 90 | 1259 | 34 | 1259 | 338 | 338 | 190 | 1 | 28 | 29 | 32 |
| 81 | HPTRF90 | 209086 05/29/97 | pBluescript | 91 | 1566 | 450 | 1552 | 593 | 593 | 191 | 1 | 28 | 29 | 83 |
| 82 | HSRDH01 | 209086 05/29/97 | Uni-ZAP XR | 92 | 1593 | 107 | 1593 | 379 | 379 | 192 | 1 | 22 | 23 | 122 |
| 83 | HSAWD74 | 209126 06/19/97 | Uni-ZAP XR | 93 | 970 | 106 | 970 | 142 | 142 | 193 | 1 | 26 | 27 | 142 |

| Gene No. | cDNA Clone ID | ATCC Deposit Nr and Date | Vector | NT SEQ ID NO: X | Total NT Seq. | 5' NT of Clone Seq. | 3' NT of Clone Seq. | 5' NT of Start Codon | 5' NT of First AA of Signal Pep | AA SEQ ID NO: Y | First AA of Sig Pep | Last AA of Sig Pep | First AA of Secreted Portion | Last AA of ORF |
|----------|---------------|--------------------------|------------|-----------------|---------------|---------------------|---------------------|----------------------|---------------------------------|-----------------|---------------------|--------------------|------------------------------|----------------|
| 83 | HSTBE27 | 209086 05/29/97 | Uni-ZAP XR | 110 | 646 | 117 | 646 | 122 | 122 | 210 | 1 | 31 | 32 | 46 |
| 84 | HTEJO12 | 209086 05/29/97 | Uni-ZAP XR | 94 | 934 | 1 | 934 | 202 | 202 | 194 | 1 | 20 | 21 | 50 |
| 85 | HTLAB43 | 209086 05/29/97 | Uni-ZAP XR | 95 | 1392 | 199 | 1392 | 384 | 384 | 195 | 1 | 17 | 18 | 221 |
| 86 | HTWCT03 | 209086 05/29/97 | pSport1 | 96 | 1963 | 1 | 1963 | 334 | 334 | 196 | 1 | 26 | 27 | 101 |

Table 1 summarizes the information corresponding to each "Gene No." described above. The nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the "cDNA clone ID" identified in Table 1 and, in some cases, from additional related DNA clones. The
5 overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X.

The cDNA Clone ID was deposited on the date and given the corresponding deposit number listed in "ATCC Deposit No:Z and Date." Some of the deposits contain
10 multiple different clones corresponding to the same gene. "Vector" refers to the type of vector contained in the cDNA Clone ID.

"Total NT Seq." refers to the total number of nucleotides in the contig identified by "Gene No." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5' NT of Clone Seq." and the "3' NT
15 of Clone Seq." of SEQ ID NO:X. The nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5' NT of Start Codon." Similarly, the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5' NT of First AA of Signal Pep."

The translated amino acid sequence, beginning with the methionine, is identified
20 as "AA SEQ ID NO:Y," although other reading frames can also be easily translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

The first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of Sig Pep" and "Last AA of Sig Pep." The predicted
25 first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion." Finally, the amino acid position of SEQ ID NO:Y of the last amino acid in the open reading frame is identified as "Last AA of ORF."

SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and
30 otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic
35 methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to the secreted proteins encoded by the cDNA clones identified in Table 1.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1. The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, or the deposited clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are species homologs. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for the desired homologue.

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below).

It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

- 5 The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified by the one-step method described in Smith and Johnson, *Gene* 67:31-40 (1988). Polypeptides of the invention also can be purified from natural or recombinant sources using antibodies of the invention raised against the secreted protein in methods which are well known in the art.
- 10

Signal Sequences

- Methods for predicting whether a protein has a signal sequence, as well as the cleavage point for that sequence, are available. For instance, the method of McGeoch, *Virus Res.* 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, *Nucleic Acids Res.* 14:4683-4690 (1986) uses the information from the residues surrounding the cleavage site, typically residues -13 to +2, where +1 indicates the amino terminus of the secreted protein. The accuracy of predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, *supra*.) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.
- 15
- 20

- In the present case, the deduced amino acid sequence of the secreted polypeptide was analyzed by a computer program called SignalP (Henrik Nielsen et al., *Protein Engineering* 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results shown in Table 1.
- 25
- 30

- As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty. Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO:Y which have an N-terminus beginning within 5 residues (i.e., + or - 5 residues) of the predicted cleavage point. Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely
- 35

uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Polynucleotide and Polypeptide Variants

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

By a polynucleotide having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the polynucleotide is identical to the reference sequence except that the polynucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a polynucleotide having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence shown in Table 1, the ORF (open reading frame), or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization

Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query

- amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions,
- 5 interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

- As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequences shown in Table 1 or to the amino acid sequence encoded by deposited DNA clone can be
- 10 determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and
- 15 subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window
- 20 Size=500 or the length of the subject amino acid sequence, whichever is shorter.

- If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity.
- 25 For subject sequences truncated at the N- and C-termini, relative to the the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of
- 30 the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are
- 35 considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the secreted protein without substantial loss of biological function. The authors of Ron et al., *J. Biol. Chem.* 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after

deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., *J. Biotechnology* 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (*J. Biol. Chem* 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

Thus, the invention further includes polypeptide variants which show substantial biological activity. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity. For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie, J. U. et al., *Science* 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

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Polynucleotide and Polypeptide Fragments

In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence contained in the deposited clone or shown in SEQ ID NO:X. The short nucleotide fragments are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in the deposited clone or the nucleotide sequence shown in SEQ ID NO:X. These nucleotide fragments are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments having a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, or 2001 to the end of SEQ ID NO:X or the cDNA contained in the deposited clone. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity. More preferably, these polynucleotides can be used as probes or primers as discussed herein.

In the present invention, a "polypeptide fragment" refers to a short amino acid sequence contained in SEQ ID NO:Y or encoded by the cDNA contained in the deposited clone. Protein fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, or 161 to the end of the coding region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the

carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotide fragments encoding these polypeptide fragments are also preferred.

Particularly, N-terminal deletions of the polypeptide of the present invention can be described by the general formula m-p, where p is the total number of amino acids in the polypeptide and m is an integer from 2 to (p-1), and where both of these integers (m & p) correspond to the position of the amino acid residue identified in SEQ ID NO:Y.

Moreover, C-terminal deletions of the polypeptide of the present invention can also be described by the general formula 1-n, where n is an integer from 2 to (p-1), and again where these integers (n & p) correspond to the position of the amino acid residue identified in SEQ ID NO:Y.

The invention also provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of SEQ ID NO:Y, where m and n are integers as described above.

Also preferred are polypeptide and polynucleotide fragments characterized by structural or functional domains, such as fragments that comprise alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet-forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions. Polypeptide fragments of SEQ ID NO:Y falling within conserved domains are specifically contemplated by the present invention. Moreover, polynucleotide fragments encoding these domains are also contemplated.

Other preferred fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Epitopes & Antibodies

In the present invention, "epitopes" refer to polypeptide fragments having antigenic or immunogenic activity in an animal, especially in a human. A preferred embodiment of the present invention relates to a polypeptide fragment comprising an

epitope, as well as the polynucleotide encoding this fragment. A region of a protein molecule to which an antibody can bind is defined as an "antigenic epitope." In contrast, an "immunogenic epitope" is defined as a part of a protein that elicits an antibody response. (See, for instance, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998-4002 (1983).)

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

In the present invention, antigenic epitopes preferably contain a sequence of at least seven, more preferably at least nine, and most preferably between about 15 to about 30 amino acids. Antigenic epitopes are useful to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe, J. G. et al., Science 219:660-666 (1983).)

Similarly, immunogenic epitopes can be used to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow, M. et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle, F. J. et al., J. Gen. Virol. 66:2347-2354 (1985).) A preferred immunogenic epitope includes the secreted protein. The immunogenic epitopes may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if it is long enough (at least about 25 amino acids), without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting.)

As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is meant to include intact molecules as well as antibody fragments (such as, for example, Fab and F(ab')₂ fragments) which are capable of specifically binding to protein. Fab and F(ab')₂ fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding than an intact antibody. (Wahl et al., J. Nucl. Med. 24:316-325 (1983).) Thus, these fragments are preferred, as well as the products of a FAB or other immunoglobulin expression library. Moreover, antibodies of the present invention include chimeric, single chain, and humanized antibodies.

Fusion Proteins

Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the

polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, the polypeptides of the present invention can be used as targeting molecules once fused to other proteins.

- 5 Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

- 10 Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final
15 preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

- 20 Moreover, polypeptides of the present invention, including fragments, and specifically epitopes, can be combined with parts of the constant domain of immunoglobulins (IgG), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life in vivo. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-
25 polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP A 394,827; Traunecker et al., Nature 331:84-86 (1988).) Fusion proteins having disulfide-linked dimeric structures (due to the IgG)
30 can also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995).)

- 35 Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the
40 fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D.

Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).

- Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein.
- Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein. (Wilson et al., Cell 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

15 Vectors, Host Cells, and Protein Production

- The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

- The polynucleotides may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

- The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

- As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance

genes for culturing in *E. coli* and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as *E. coli*, *Streptomyces* and *Salmonella typhimurium* cells; fungal cells, such as yeast cells; insect cells such as *Drosophila* S2 and *Spodoptera Sf9* cells; animal cells such as CHO, COS, 5 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and 10 ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Other suitable vectors will be readily apparent to the skilled artisan.

Introduction of the construct into the host cell can be effected by calcium 15 phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., *Basic Methods In Molecular Biology* (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

20 A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most 25 preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention, and preferably the secreted form, can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic 30 procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial 35 modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein

after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

5

Uses of the Polynucleotides

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

10

The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each polynucleotide of the present invention can be used as a chromosome marker.

15

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the SEQ ID NO:X will yield an amplified fragment.

20

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, and preselection by hybridization to construct chromosome specific-cDNA libraries.

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Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

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For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes). Preferred polynucleotides correspond to the noncoding regions of the cDNAs because the coding sequences are

more likely conserved within gene families, thus increasing the chance of cross hybridization during chromosomal mapping.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) .) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in the polynucleotide and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using polynucleotides of the present invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

In addition to the foregoing, a polynucleotide can be used to control gene expression through triple helix formation or antisense DNA or RNA. Both methods rely on binding of the polynucleotide to DNA or RNA. For these techniques, preferred polynucleotides are usually 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques are effective in model

systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of

unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to particular tissue prepared from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination.

5 In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers
10 for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

Uses of the Polypeptides

Each of the polypeptides identified herein can be used in numerous ways. The
15 following description should be considered exemplary and utilizes known techniques.

A polypeptide of the present invention can be used to assay protein levels in a biological sample using antibody-based techniques. For example, protein expression in tissues can be studied with classical immunohistological methods. (Jalkanen, M., et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell . Biol. 105:3087-
20 3096 (1987).) Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and
25 technetium (99mTc), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying secreted protein levels in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-
30 radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

35 A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, 131I, 112In, 99mTc), a radio-opaque substance, or a material detectable by nuclear magnetic

resonance, is introduced (for example, parenterally, subcutaneously, or intraperitoneally) into the mammal. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human
5 subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of ^{99m}Tc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The
10 Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).)

Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression of a polypeptide of the present invention in cells or body fluid of an individual; (b) comparing the level of gene expression with a standard gene
15 expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a disorder.

Moreover, polypeptides of the present invention can be used to treat disease. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to
20 supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B), to inhibit the activity of a polypeptide (e.g., an oncogene), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired
25 response (e.g., blood vessel growth).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease. For example, administration of an antibody directed to a polypeptide of the present invention can bind and reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such
30 as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a
35 recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

Biological Activities

The polynucleotides and polypeptides of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides could be used to treat the associated disease.

Immune Activity

10 A polypeptide or polynucleotide of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, a polynucleotide or polypeptide of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

20 A polynucleotide or polypeptide of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells. A polypeptide or polynucleotide of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

Moreover, a polypeptide or polynucleotide of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, a polynucleotide or polypeptide of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, a polynucleotide or polypeptide of the present invention that can

decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

5 A polynucleotide or polypeptide of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation,
10 differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected by the present invention include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis,
15 glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitus, and autoimmune
20 inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by a polypeptide or polynucleotide of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

25 A polynucleotide or polypeptide of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The
30 administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, a polypeptide or polynucleotide of the present invention may also be used to modulate inflammation. For example, the polypeptide or polynucleotide may
35 inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including inflammation associated with infection (e.g., septic

shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

Hyperproliferative Disorders

A polypeptide or polynucleotide can be used to treat or detect hyperproliferative disorders, including neoplasms. A polypeptide or polynucleotide of the present invention may inhibit the proliferation of the disorder through direct or indirect interactions. Alternatively, a polypeptide or polynucleotide of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but are not limited to neoplasms located in the: abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstrom's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

Infectious Disease

A polypeptide or polynucleotide of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases

may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, the polypeptide or polynucleotide of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

- 5 Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of viruses, include, but are not limited to the following DNA and RNA viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza), Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiolitis, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox, hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

- 25 Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following Gram-Negative and Gram-positive bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia, Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, Enterobacteriaceae (Klebsiella, Salmonella, Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Meningococcal), Pasteurellaceae Infections (e.g., Actinobacillus, Haemophilus, Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, 30 and Staphylococcal. These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS

- related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis, Chlamydia, Syphilis, Diphtheria,
- 5 Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.
- 10 Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following families: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas.
- 15 These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related), Malaria, pregnancy complications, and toxoplasmosis. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or
- 20 diseases.

- Preferably, treatment using a polypeptide or polynucleotide of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo
- 25 therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

Regeneration

- A polynucleotide or polypeptide of the present invention can be used to
- 30 differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteoarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion
- 35 injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal

or cardiac), vascular (including vascular endothelium), nervous, hematopoietic, and skeletal (bone, cartilage, tendon and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, a polynucleotide or polypeptide of the present invention may increase
5 regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. A polynucleotide or polypeptide of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tendon or ligament defects. A further example of tissue
10 regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using a polynucleotide or polypeptide of the present invention to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and
15 peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stroke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease,
20 Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotide or polypeptide of the present invention.

Chemotaxis

25 A polynucleotide or polypeptide of the present invention may have chemotaxis activity. A chemotactic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular
30 trauma or abnormality.

A polynucleotide or polypeptide of the present invention may increase chemotactic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body.
35 For example, chemotactic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that a polynucleotide or polypeptide of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, a polynucleotide or polypeptide of the present invention could be used as an inhibitor of chemotaxis.

5

Binding Activity

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit (antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors), or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide, either as a secreted protein or on the cell membrane. Preferred cells include cells from mammals, yeast, *Drosophila*, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

5 All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptide from suitably manipulated cells or tissues.

10 Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with
15 a polypeptide of the invention, (b) assaying a biological activity, and (b) determining if a biological activity of the polypeptide has been altered.

Other Activities

20 A polypeptide or polynucleotide of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide or polynucleotide of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic
25 surgery). Similarly, a polypeptide or polynucleotide of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

A polypeptide or polynucleotide of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, cardiac
30 rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

A polypeptide or polynucleotide of the present invention may also be used as a
35 food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

Other Preferred Embodiments

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Clone Sequence and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Start Codon and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Similarly preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X.

Also preferred is an isolated nucleic acid molecule which hybridizes under
5 stringent hybridization conditions to a nucleic acid molecule, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which
10 comprises a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the material deposited with the American Type Culture Collection and given the ATCC Deposit Number shown in Table 1 for said cDNA Clone Identifier.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide
15 sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the deposit given the ATCC Deposit Number shown in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at
20 least 50 contiguous nucleotides is included in the nucleotide sequence of the complete open reading frame sequence encoded by said human cDNA clone.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

25 A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide
30 sequence encoded by said human cDNA clone.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer
35 as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method

comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

- 5 Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined
10 from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

- A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95%
15 identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

- 20 The method for identifying the species, tissue or cell type of a biological sample can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

- 25 Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous
30 nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

- 35 The method for diagnosing a pathological condition can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95%

identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1.

Also preferred is a polypeptide, wherein said sequence of contiguous amino acids is included in the amino acid sequence of SEQ ID NO:Y in the range of positions beginning with the residue at about the position of the First Amino Acid of the Secreted Portion and ending with the residue at about the Last Amino Acid of the Open Reading Frame as set forth for SEQ ID NO:Y in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a secreted portion of the secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method for detecting in a biological sample a polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide

comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone
5 identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

10 Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as
15 defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide
20 molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition
25 associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a
30 sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

35 In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a secreted portion of a human secreted protein comprising an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y beginning with the residue at the position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y wherein Y is an integer set forth in Table 1 and said position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y is defined in Table 1; and an amino acid sequence of a secreted portion of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a secreted protein activity, which method comprises administering to such an individual a pharmaceutical composition comprising an amount of an isolated polypeptide, polynucleotide, or antibody of the claimed invention effective to increase the level of said protein activity in said individual.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

10

Examples

Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample

Each cDNA clone in a cited ATCC deposit is contained in a plasmid vector. Table 1 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The table immediately below correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 1 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

| <u>Vector Used to Construct Library</u> | <u>Corresponding Deposited Plasmid</u> |
|---|--|
| Lambda Zap | pBluescript (pBS) |
| Uni-Zap XR | pBluescript (pBS) |
| Zap Express | pBK |
| lafmid BA | plafmid BA |
| pSport1 | pSport1 |
| pCMVSPORT 2.0 | pCMVSPORT 2.0 |
| pCMVSPORT 3.0 | pCMVSPORT 3.0 |
| pCR [®] 2.1 | pCR [®] 2.1 |

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1

Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS. The S and K refers to the orientation of the polylinker to the T7 and T3 primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the f1 origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the f1 ori generates sense strand DNA and in the other, antisense.

Vectors pSport1, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993).) Vector lacmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR[®]2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 1, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited in Table 1 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone identified in Table 1. Typically, each ATCC deposit sample cited in Table 1 comprises a mixture of approximately equal amounts (by weight) of about 50 plasmid DNAs, each containing a different cDNA clone; but such a deposit sample may include plasmids for more or less than 50 cDNA clones, up to about 500 cDNA clones.

Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 1. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to SEQ ID NO:X.

Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with ³²P-γ-ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring, NY (1982).)

The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

Alternatively, two primers of 17-20 nucleotides derived from both ends of the SEQ ID NO:X (i.e., within the region of SEQ ID NO:X bounded by the 5' NT and the 3' NT of the clone defined in Table 1) are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 μ l of reaction mixture with 0.5 μ g of the above cDNA template. A convenient reaction mixture is 1.5-5 mM $MgCl_2$, 0.01% (w/v) gelatin, 20 μ M each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., *Nucleic Acids Res.* 21(7):1683-1684 (1993).)

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then
5 be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA
10 synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

15

Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR
20 using primers selected for the cDNA sequence corresponding to SEQ ID NO:X., according to the method described in Example 1. (See also, Sambrook.)

Example 3: Tissue Distribution of Polypeptide

Tissue distribution of mRNA expression of polynucleotides of the present invention is determined using protocols for Northern blot analysis, described by,
25 among others, Sambrook et al. For example, a cDNA probe produced by the method described in Example 1 is labeled with P³² using the rediprime™ DNA labeling system (Amersham Life Science), according to manufacturer's instructions. After labeling, the probe is purified using CHROMA SPIN-100™ column (Clontech Laboratories, Inc.), according to manufacturer's protocol number PT1200-1. The purified labeled probe is
30 then used to examine various human tissues for mRNA expression.

Multiple Tissue Northern (MTN) blots containing various human tissues (H) or human immune system tissues (IM) (Clontech) are examined with the labeled probe using ExpressHyb™ hybridization solution (Clontech) according to manufacturer's protocol number PT1190-1. Following hybridization and washing, the blots are
35 mounted and exposed to film at -70°C overnight, and the films developed according to standard procedures.

Example 4: Chromosomal Mapping of the Polynucleotides

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions : 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

Example 5: Bacterial Expression of a Polypeptide

A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp^r), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan^r). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 (O.D.⁶⁰⁰) of between 0.4 and 0.6. IPTG

(Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by
5 centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high
10 affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with
15 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in
20 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM imidazole. Imidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

25 In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of
30 replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (lacIq). The origin of replication (oriC) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and
35 XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA

insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

- 5 The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

Example 6: Purification of a Polypeptide from an Inclusion Body

- 10 The following alternative method can be used to purify a polypeptide expressed in *E. coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

- Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

- 20 The cells are then lysed by passing the solution through a microfluidizer (Microfluidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

- 25 The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

- 30 Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

 To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area

(e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A_{280} monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5 μ g of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

Example 7: Cloning and Expression of a Polypeptide in a Baculovirus

Expression System

In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak *Drosophila* promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., Virology 170:31-39 (1989).

Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon and the naturally associated leader sequence identified in Table 1, is amplified using the PCR protocol described in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("GeneClean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("GeneClean" BIO 101 Inc., La Jolla, Ca.).

The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

Five μ g of a plasmid containing the polynucleotide is co-transfected with 1.0 μ g of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA", Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One μ g of BaculoGold™ virus DNA and 5 μ g of the plasmid are mixed in a sterile well of a microtiter plate containing 50 μ l of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10 μ l Lipofectin plus 90 μ l Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm

tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

- 5 After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.)
- 10 After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 µl of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in
- 15 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

- To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection
- 20 ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 µCi of ³⁵S-methionine and 5 µCi ³⁵S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins
- 25 in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

30 **Example 8: Expression of a Polypeptide in Mammalian Cells**

The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates

the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLVI, HIVI and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSPORT 2.0, and pCMVSPORT 3.0. Mammalian host cells that could be used include, human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as dhfr, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No. 209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the CMV-enhancer (Boshart et al., Cell 41:521-530 (1985)). Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the

polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the vector does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five μ g of the expression plasmid pC6 is cotransfected with 0.5 μ g of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of methotrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 μ M, 2 μ M, 5 μ M, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200 μ M. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

35

Example 9: Protein Fusions

The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the half-life time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

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GGGATCCGGAGCCCAAATCTTCTGACAAAACCTCACACATGCCCACCGTGCC
CAGCACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCAAAC
35 CAAGGACACCCTCATGATCTCCCGGACTCCTGAGGTACATGCGTGGTGGT
GGACGTAAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACG
GCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAAC

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AGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTG
 AATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAACCCCC
 ATCGAGAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCAAGGT
 GTACACCCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCT
 5 GACCTGCCTGGTCAAAGGCTTCTATCCAAGCGACATCGCCGTGGAGTGGGA
 GAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGG
 ACTCCGACGGCTCCTTCTTCTCTACAGCAAGCTCACCGTGGACAAGAGCA
 GGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGC
 ACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAGTGC
 10 GACGGCCGCGACTCTAGAGGAT (SEQ ID NO:1)

Example 10: Production of an Antibody from a Polypeptide

The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) For example, cells expressing a polypeptide of the present invention is administered to an animal to induce the production of sera containing polyclonal antibodies. In a preferred method, a preparation of the secreted protein is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

20 In the most preferred method, the antibodies of the present invention are monoclonal antibodies (or protein binding fragments thereof). Such monoclonal antibodies can be prepared using hybridoma technology. (Köhler et al., Nature 256:495 (1975); Köhler et al., Eur. J. Immunol. 6:511 (1976); Köhler et al., Eur. J. Immunol. 6:292 (1976); Hammerling et al., in: Monoclonal Antibodies and T-Cell Hybridomas, Elsevier, N.Y., pp. 563-681 (1981).) In general, such procedures involve immunizing an animal (preferably a mouse) with polypeptide or, more preferably, with a secreted polypeptide-expressing cell. Such cells may be cultured in any suitable tissue culture medium; however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at 30 about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 µg/ml of streptomycin.

The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line 35 (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as

described by Wands et al. (Gastroenterology 80:225-232 (1981).) The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide.

Alternatively, additional antibodies capable of binding to the polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic antibodies to the protein-specific antibody and can be used to immunize an animal to induce formation of further protein-specific antibodies.

It will be appreciated that Fab and F(ab')₂ and other fragments of the antibodies of the present invention may be used according to the methods disclosed herein. Such fragments are typically produced by proteolytic cleavage, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')₂ fragments). Alternatively, secreted protein-binding fragments can be produced through the application of recombinant DNA technology or through synthetic chemistry.

For in vivo use of antibodies in humans, it may be preferable to use "humanized" chimeric monoclonal antibodies. Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric antibodies are known in the art. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

Example 11: Production Of Secreted Protein For High-Throughput Screening Assays

The following protocol produces a supernatant containing a polypeptide to be tested. This supernatant can then be used in the Screening Assays described in Examples 13-20.

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a

working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The
 5 PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

Plate 293T cells (do not carry cells past P+20) at 2×10^5 cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x
 10 Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing a polynucleotide insert, produced by the methods described in
 15 Examples 8 or 9, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of
 20 transfections.

Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off
 25 PBS rinse, and person B, using a 12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37°C for 6 hours.

While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with 1x penstrep, or CHO-5 media (116.6 mg/L of CaCl_2 (anhyd); 0.00130 mg/L
 30 $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$; 0.050 mg/L of $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$; 0.417 mg/L of $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$; 311.80 mg/L of KCl; 28.64 mg/L of MgCl_2 ; 48.84 mg/L of MgSO_4 ; 6995.50 mg/L of NaCl; 2400.0 mg/L of NaHCO_3 ; 62.50 mg/L of $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$; 71.02 mg/L of Na_2HPO_4 ; .4320 mg/L of $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$; .002 mg/L of Arachidonic Acid ; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic
 35 Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic Acid; 0.010 mg/L of Palmitic Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of

Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml of L-Asparagine-H₂O; 6.65 mg/ml of L-Aspartic Acid; 22.56 mg/ml of L-Cystine-2HCL-H₂O; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0
 5 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL-H₂O; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalanine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tyrosine-2Na-2H₂O; 99.65 mg/ml of L-Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; and 0.680 mg/L of Vitamin B₁₂; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine;
 10 0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; and 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal) with 2mm glutamine and 1x
 15 penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B
 25 adds 1.5ml appropriate media to each well. Incubate at 37°C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 13-20.

30 It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide directly (e.g., as a secreted protein) or by the polypeptide inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an
 35 activity in a particular assay.

Example 12: Construction of GAS Reporter Construct

One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proximal region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:2)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

| | <u>Ligand</u> | <u>tyk2</u> | <u>JAKs</u> <u>Jak1</u> | <u>Jak2</u> | <u>Jak3</u> | <u>STATS</u> | <u>GAS(elements) or ISRE</u> |
|----|----------------------------------|-------------|----------------------------|-------------|-------------|--------------|------------------------------|
| | <u>IFN family</u> | | | | | | |
| 5 | IFN-a/B | + | + | - | - | 1,2,3 | ISRE |
| | IFN-g | | + | + | - | 1 | GAS (IRF1>Lys6>IFP) |
| | IL-10 | + | ? | ? | - | 1,3 | |
| | <u>gp130 family</u> | | | | | | |
| 10 | IL-6 (Pleiotrohic) | + | + | + | ? | 1,3 | GAS (IRF1>Lys6>IFP) |
| | IL-11(Pleiotrohic) | ? | + | ? | ? | 1,3 | |
| | OnM(Pleiotrohic) | ? | + | + | ? | 1,3 | |
| | LIF(Pleiotrohic) | ? | + | + | ? | 1,3 | |
| | CNTF(Pleiotrohic) | -/+ | + | + | ? | 1,3 | |
| 15 | G-CSF(Pleiotrohic) | ? | + | ? | ? | 1,3 | |
| | IL-12(Pleiotrohic) | + | - | + | + | 1,3 | |
| | <u>g-C family</u> | | | | | | |
| 20 | IL-2 (lymphocytes) | - | + | - | + | 1,3,5 | GAS |
| | IL-4 (lymph/myeloid) | - | + | - | + | 6 | GAS (IRF1 = IFP >>Ly6)(IgH) |
| | IL-7 (lymphocytes) | - | + | - | + | 5 | GAS |
| | IL-9 (lymphocytes) | - | + | - | + | 5 | GAS |
| | IL-13 (lymphocyte) | - | + | ? | ? | 6 | GAS |
| | IL-15 | ? | + | ? | + | 5 | GAS |
| 25 | <u>gp140 family</u> | | | | | | |
| | IL-3 (myeloid) | - | - | + | - | 5 | GAS (IRF1>IFP>>Ly6) |
| | IL-5 (myeloid) | - | - | + | - | 5 | GAS |
| 30 | GM-CSF (myeloid) | - | - | + | - | 5 | GAS |
| | <u>Growth hormone family</u> | | | | | | |
| | GH | ? | - | + | - | 5 | |
| | PRL | ? | +/- | + | - | 1,3,5 | |
| | EPO | ? | - | + | - | 5 | GAS(B-CAS>IRF1=IFP>>Ly6) |
| 35 | <u>Receptor Tyrosine Kinases</u> | | | | | | |
| | EGF | ? | + | + | - | 1,3 | GAS (IRF1) |
| | PDGF | ? | + | + | - | 1,3 | |
| 40 | CSF-1 | ? | + | + | - | 1,3 | GAS (not IRF1) |

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 13-14, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:

5':GCGCCTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCG
 10 AAATGATTTCCTCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:3)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTGTCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:

5':CTCGAGATTTCCTCCGAAATCTAGATTTCCTCCGAAATGATTTCCTCCGAAATG
 20 ATTTTCCTCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCC
 CTAAGTCCGCCCCTCCGCCCCTAAGTCCGCCCAGTTCGCCCATTCTCCGC
 CCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCTCGGC
 CTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTT
 TGCAAAAAGCTT:3' (SEQ ID NO:5)

25 With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol acetyltransferase (CAT), luciferase,
 30 alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a
 35 neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 13-14.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 15 and 16. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, IL-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

Example 13: High-Throughput Screening Assay for T-cell Activity.

The following protocol is used to assess T-cell activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate T-cells. T-cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml gentamicin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies)

with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

During the incubation period, count cell concentration, spin down the required number of cells (10^7 per transfection), and resuspend in OPTI-MEM to a final
5 concentration of 10^7 cells/ml. Then add 1ml of 1×10^7 cells in OPTI-MEM to T25 flask and incubate at 37°C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Genticin, and 1% Pen-Strep. These cells are treated with supernatants containing a polypeptide as produced by the protocol described in Example 11.

10 On the day of treatment with the supernatant, the cells should be washed and resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

15 Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12
20 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples
25 from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20°C until SEAP assays are performed according to Example 17. The plates containing the remaining treated cells are placed at 4°C and serve as a source of material for repeating the assay on a specific well if desired.

30 As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

Example 14: High-Throughput Screening Assay Identifying Myeloid Activity

The following protocol is used to assess myeloid activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate myeloid cells.

- 5 Myeloid cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

- 10 To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 12, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2×10^7 U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

- 15 Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$, 1 mM MgCl_2 , and 675 uM CaCl_2 . Incubate at 37°C for 45 min.

- 20 Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37°C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

- 25 These cells are tested by harvesting 1×10^8 cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of 5×10^5 cells/ml. Plate 200 ul cells per well in the 96-well plate (or 1×10^5 cells/well).

- 30 Add 50 ul of the supernatant prepared by the protocol described in Example 11. Incubate at 37°C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 17.

Example 15: High-Throughput Screening Assay Identifying Neuronal Activity.

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:6)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:7)

Using the GAS:SEAP/Neo vector produced in Example 12, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 11. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine

growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS (Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as 5×10^5 cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to 1×10^5 cells/well). Add 50 ul supernatant produced by Example 11, 37°C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 17.

Example 16: High-Throughput Screening Assay for T-cell Activity

NF- κ B (Nuclear Factor κ B) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF- κ B regulates the expression of genes involved in immune cell activation, control of apoptosis (NF- κ B appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- κ B is retained in the cytoplasm with I- κ B (Inhibitor κ B). However, upon stimulation, I- κ B is phosphorylated and degraded, causing NF- κ B to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- κ B include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF- κ B promoter element are used to screen the supernatants produced in Example 11. Activators or inhibitors of NF- κ B would be useful in treating

diseases. For example, inhibitors of NF- κ B could be used to treat those diseases related to the acute or chronic activation of NF- κ B, such as rheumatoid arthritis.

To construct a vector containing the NF- κ B promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF- κ B binding site (GGGGACTTTCCC) (SEQ ID NO:8), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:
5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGAC
TTTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:9)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:
5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene)
Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTCC
ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCCTAACTCCGCCCCA
TCCCGCCCCCTAACTCCGCCCCAGTTCCGCCCCATTCTCCGCCCCATGGCTGACT
AATTTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTC
CAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTT:
3' (SEQ ID NO:10)

Next, replace the SV40 minimal promoter element present in the pSEAP2- promoter plasmid (Clontech) with this NF- κ B/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF- κ B/SV40/SEAP cassette is removed from the above NF- κ B/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the NF- κ B/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

Once NF- κ B/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 13. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described in Example 13. As a positive control, exogenous TNF alpha (0.1, 1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

Example 17: Assay for SEAP Activity

As a reporter molecule for the assays described in Examples 13-16, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 μ l of 2.5x dilution buffer into Optiplates containing 35 μ l of a supernatant. Seal the plates with a plastic sealer and incubate at 65°C for 30 min. Separate the Optiplates to avoid uneven heating.

Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 μ l Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 μ l Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

Reaction Buffer Formulation:

| # of plates | Rxn buffer diluent (ml) | CSPD (ml) |
|-------------|-------------------------|-----------|
| 10 | 60 | 3 |
| 11 | 65 | 3.25 |
| 12 | 70 | 3.5 |
| 13 | 75 | 3.75 |
| 14 | 80 | 4 |
| 15 | 85 | 4.25 |
| 16 | 90 | 4.5 |
| 17 | 95 | 4.75 |
| 18 | 100 | 5 |
| 19 | 105 | 5.25 |
| 20 | 110 | 5.5 |
| 21 | 115 | 5.75 |
| 22 | 120 | 6 |

| | | |
|----|-----|-------|
| 23 | 125 | 6.25 |
| 24 | 130 | 6.5 |
| 25 | 135 | 6.75 |
| 26 | 140 | 7 |
| 27 | 145 | 7.25 |
| 28 | 150 | 7.5 |
| 29 | 155 | 7.75 |
| 30 | 160 | 8 |
| 31 | 165 | 8.25 |
| 32 | 170 | 8.5 |
| 33 | 175 | 8.75 |
| 34 | 180 | 9 |
| 35 | 185 | 9.25 |
| 36 | 190 | 9.5 |
| 37 | 195 | 9.75 |
| 38 | 200 | 10 |
| 39 | 205 | 10.25 |
| 40 | 210 | 10.5 |
| 41 | 215 | 10.75 |
| 42 | 220 | 11 |
| 43 | 225 | 11.25 |
| 44 | 230 | 11.5 |
| 45 | 235 | 11.75 |
| 46 | 240 | 12 |
| 47 | 245 | 12.25 |
| 48 | 250 | 12.5 |
| 49 | 255 | 12.75 |
| 50 | 260 | 13 |

Example 18: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-3, used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO₂ incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-3 is made in 10% pluronic acid DMSO. To load the cells with fluo-3, 50 ul of 12 ug/ml fluo-3 is added to each well. The plate is incubated at 37°C in a CO₂ incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

- 5 For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10⁶ cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-3 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37°C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10⁶ cells/ml, and dispensed into a microplate, 100
10 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley CellWash with 200 ul, followed by an aspiration step to 100 ul final volume.

For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-3. The supernatant is added to the well, and a change in fluorescence is detected.

- To measure the fluorescence of intracellular calcium, the FLIPR is set for the
15 following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event which has resulted in an increase in the intracellular Ca⁺⁺ concentration.

20

Example 19: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity

- The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase
25 RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

- 30 Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members
35 of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, the identification of novel human secreted proteins capable of activating tyrosine kinase signal transduction pathways are of interest. Therefore, the following protocol is designed to identify those novel human secreted proteins capable of
5 activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr
10 with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford, MA), or calf serum, rinsed with PBS and stored at 4°C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of
15 alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford, MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of
20 Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 11, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na₃VO₄, 2 mM Na₄P₂O₇
25 and a cocktail of protease inhibitors (# 1836170) obtained from Boehringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum
30 manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4°C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

35 Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a

biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

- 5 The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg₂₊ (5mM ATP/50mM MgCl₂), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM MgCl₂, 5 mM MnCl₂, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the
- 10 components gently and preincubate the reaction mix at 30°C for 2 min. Initiate the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mM EDTA and place the reactions on ice.

- Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction
- 15 mixture to a microtiter plate (MTP) module and incubating at 37°C for 20 min. This allows the streptavidin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phosphotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37°C for one hour. Wash the well as
- 20 above.

- Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of
- 25 tyrosine kinase activity.

Example 20: High-Throughput Screening Assay Identifying Phosphorylation Activity

- As a potential alternative and/or complement to the assay of protein tyrosine
- 30 kinase activity described in Example 19, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase,
- 35 Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other

phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then
5 rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4°C
10 until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 11 for 5-20 minutes. The cells are then solubilized and extracts
15 filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and
20 Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation.

25

Example 21: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from
30 these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky, D., et al., Science 252:706 (1991).

35 PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies).

The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

5 PCR products is cloned into T-tailed vectors as described in Holton, T.A. and Graham, M.W., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

10 Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenin deoxy-uridine 5'-triphosphate (Boehringer Mannheim), and FISH performed as described in Johnson, Cg. et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

15 Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson, Cv. et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and
20 chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated
25 disease.

Example 22: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

30 A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

35 For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10.

The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

Example 23: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1 µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1 µg/kg/hour to about 50 µg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracisternally, intravaginally,

intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), buccally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semi-permeable polymer matrices in the form of shaped articles, e.g., films, or microcapsules. Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., *Biopolymers* 22:547-556 (1983)), poly (2-hydroxyethyl methacrylate) (R. Langer et al., *J. Biomed. Mater. Res.* 15:167-277 (1981), and R. Langer, *Chem. Tech.* 12:98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D-(-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE 3,218,121; Epstein et al., *Proc. Natl. Acad. Sci. USA* 82:3688-3692 (1985); Hwang et al., *Proc. Natl. Acad. Sci. USA* 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides.

Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

Example 24: Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form.

- 5 Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily
10 dose 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 23.

Example 25: Method of Treating Increased Levels of the Polypeptide

- 15 Antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5,
20 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 23.

Example 26: Method of Treatment Using Gene Therapy

- 25 One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is
30 turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

Example 27: Method of Treatment Using Gene Therapy - In Vivo

Another aspect of the present invention is using *in vivo* gene therapy methods to treat disorders, diseases and conditions. The gene therapy method relates to the introduction of naked nucleic acid (DNA, RNA, and antisense
5 DNA or RNA) sequences into an animal to increase or decrease the expression of the polypeptide of the present invention. A polynucleotide of the present invention may be operatively linked to a promoter or any other genetic elements necessary for the expression of the encoded polypeptide by the target tissue. Such gene therapy and delivery techniques and methods are known in the art,
10 see, for example, WO90/11092, WO98/11779; U.S. Patent NO. 5693622, 5705151, 5580859; Tabata H. et al. (1997) Cardiovasc. Res. 35(3):470-479, Chao J et al. (1997) Pharmacol. Res. 35(6):517-522, Wolff J.A. (1997) Neuromuscul. Disord. 7(5):314-318, Schwartz B. et al. (1996) Gene Ther. 3(5):405-411, Tsurumi Y. et al. (1996) Circulation 94(12):3281-3290
15 (incorporated herein by reference).

The polynucleotide constructs of the present invention may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). These polynucleotide constructs can be delivered in a
20 pharmaceutically acceptable liquid or aqueous carrier.

The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the
25 polynucleotides may also be delivered in liposome formulations (such as those taught in Felgner P.L. et al. (1995) Ann. NY Acad. Sci. 772:126-139 and Abdallah B. et al. (1995) Biol. Cell 85(1):1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs of the present invention used in
30 the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the
35 transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

The polynucleotide construct of the present invention can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or RNA will be in the range of from about 0.05 g/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for the polypeptide of the present invention is prepared in accordance with a standard recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with

liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about 0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e.g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice. The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA of the present invention.

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference.

Sequence Listing

(1) GENERAL INFORMATION:

5

(i) APPLICANT: Rosen et al.

(ii) TITLE OF INVENTION: 86 Human Secreted Proteins

10

(iii) NUMBER OF SEQUENCES: 318

(iv) CORRESPONDENCE ADDRESS:

15

(A) ADDRESSEE: Human Genome Sciences, Inc.

(B) STREET: 9410 Key West Avenue

(C) CITY: Rockville

20

(D) STATE: Maryland

(E) COUNTRY: USA

25

(F) ZIP: 20850

(v) COMPUTER READABLE FORM:

30

(A) MEDIUM TYPE: Diskette, 3.50 inch, 1.4Mb storage

(B) COMPUTER: HP Vectra 486/33

35

(C) OPERATING SYSTEM: MSDOS version 6.2

(D) SOFTWARE: ASCII Text

40

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:

45

(B) FILING DATE: June 11, 1998

(C) CLASSIFICATION:

50

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER:

55

(B) FILING DATE:

(viii) ATTORNEY/AGENT INFORMATION:

- 5 (A) NAME: A. Anders Brookes
(B) REGISTRATION NUMBER: 36,373
10 (C) REFERENCE/DOCKET NUMBER: PZ008PCT

(vi) TELECOMMUNICATION INFORMATION:

- 15 (A) TELEPHONE: (301) 309-8504
(B) TELEFAX: (301) 309-8439
20

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 733 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

GGGATCCGGA GCCCAAATCT TCTGACAAAA CTCACACATG CCCACCGTGC CCAGCACCTG 60
AATTCGAGGG TGCACCGTCA GTCTTCCTCT TCCCCC AAA ACCCAAGGAC ACCCTCATGA 120
35 TCTCCCGGAC TCCTGAGGTC ACATGCGTGG TGGTGGACGT AAGCCACGAA GACCTGAGG 180
TCAAGTTCAA CTGGTACGTG GACGGCGTGG AGGTGCATAA TGCCAAGACA AAGCCGCGGG 240
40 AGGAGCAGTA CAACAGCACG TACCGTGTGG TCAGCGTCCT CACCGTCCTG CACCAGGACT 300
GGCTGAATGG CAAGGAGTAC AAGTGCAAGG TCTCCAACAA AGCCCTCCCA ACCCCCATCG 360
AGAAAACCAT CTCCAAGCC AAAGGGCAGC CCCGAGAACC ACAGGTGTAC ACCCTGCCCC 420
45 CATCCCGGGA TGAGCTGACC AAGAACCAGG TCAGCCTGAC CTGCCTGGTC AAAGGCTTCT 480
ATCCAAGCGA CATGCGCGTG GAGTGGGAGA GCAATGGGCA GCCGGAGAAC AACTACAAGA 540
50 CCACGCCTCC CGTGCTGGAC TCCGACGGCT CCTTCTTCCT CTACAGCAAG CTCACCGTGG 600
ACAAGAGCAG GTGGCAGCAG GGAACGTCT TCTCATGCTC CGTGATGCAT GAGGCTCTGC 660
ACAACCACTA CACGCAGAAG AGCCTCTCCC TGTCTCCGGG TAAATGAGTG CGACGGCCGC 720
55 GACTCTAGAG GAT 733

(2) INFORMATION FOR SEQ ID NO: 2:

- 5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Trp Ser Xaa Trp Ser
1 5

15

(2) INFORMATION FOR SEQ ID NO: 3:

- 20 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 86 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
25 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

GCGCCTCGAG ATTTCCCCGA AATCTAGATT TCCCCGAAAT GATTTCCTCG AAATGATTTC 60
30 CCCGAAATAT CTGCCATCTC AATTAG 86

35 (2) INFORMATION FOR SEQ ID NO: 4:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
40 (C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

45 GCGGCAAGCT TTTTGCAAAG CCTAGGC 27

50 (2) INFORMATION FOR SEQ ID NO: 5:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 271 base pairs
(B) TYPE: nucleic acid
55 (C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

60 CTCGAGATTT CCCCAGAAATC TAGATTTCCT CGAAATGATT TCCCCGAAAT GATTTCCTCG 60

AAA'ATCTGC CATCTCAATT AGTCAGCAAC CATAGTCCCG CCCCTAACTC CGCCCATCCC 120
GCCCCTAACT CGCCCCAGTT CGCCCCATTC TCGCCCCAT GGCTGACTAA TTTTTTTTAT 180
5 TTATGCAGAG GCCGAGGCCG CCTCGGCCTC TGAGCTATTC CAGAAGTAGT GAGGAGGCTT 240
TTTTGGAGGC CTAGGCTTTT GCAAAAAGCT T 271
10

(2) INFORMATION FOR SEQ ID NO: 6:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:
GCGCTCGAGG GATGACAGCG ATAGAACCCC GG 32

25

(2) INFORMATION FOR SEQ ID NO: 7:

30 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:
GCGAAGCTTC GCGACTCCCC GGATCCGCCT C 31
40

45

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
50 (D) TOPOLOGY: linear
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:
GGGGACTTTC CC 12
55

60

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 73 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

GCGGCCTCGA GGGGACTTTC CCGGGGACTT TCCGGGGACT TTCGGGACT TTCCATCCTG 60
CCATCTCAAT TAG 73

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 256 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

CTCGAGGGGA CTTTCCGGG GACTTTCGG GGACTTTCGG GGACTTTCGA TCTGCCATCT 60
CAATTAGTCA GCAACCATAG TCCCGCCCTT AACTCCGCCC ATCCCGCCCC TAACTCCGCC 120
CAGTTCGGCC CATCTCCGC CCCATGGCTG ACTAATTTT TTTATTTATG CAGAGGCCGA 180
GGCCGCTCG GCCTCTGAGC TATTCAGAA GTAGTGAGGA GGCTTTTGTG GAGGCCTAGG 240
CTTTTGCAAA AAGCTT 256

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1220 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

CATGAATGGC TCGACAAGG ACCCCCTCCT CCCCTTTCCT GCTTCTGCGA GAACTCCCTC 60
CCTCCCTCCA GCTCCGCCAG CCCAGGCGCC CCTTCCCTGG AAGCGAGCG GCTTCGCTCG 120
CATTTACCG CCGCCGCTC TCGCAATATT GCAATATAGG GGAAAAGCAG ACCATGGTGA 180
ATCCGGGCG CAGCTCGCAG CCGCCCCCGG TGACGGCCGG CTCCTCTCC TGAAGGGT 240
GCGCAGGCTG CCGGGGCAAG ATTGCGGACC GCTTCTGCT CTATGCCATG GACAGCTATT 300
GGCACAGCG GTGCTCAAG TGCTCTGCT GCCAGGCGCA NTGGGCGACA TCGGCAGCTC 360

CTGTTACACC AAAAGTGGCA TGATCCTTTG CAGAAATGAC TACATTAGGT TATTTGGAAA 420
 TAGCGGTGCT TGCAGCGCTT GCGGACAGTC GATTCTGCG AGTGAACCTG TCATGAGGCG 480
 5 GCAAGGCAAT GTGTATCATC TTAAGTGTTC TCAATGCTCT ACCAGCCGGA ATCGCCTGGT 540
 CCGGGGAGAT CGGTTTCACT ACATCAATGG CAGTTTATTT TGTGAACATG ATAGACCTAC 600
 10 AGCTCTCATC AATGGCCATT TGAATTCATC TCARAGCAAT CCACTACTGC CAGACCAGAA 660
 GGTCTGCTAA AAGGTCAGAG TAATGCAGAA TGGGTGCCTT CATCTCAGAT TTGTTTCATCA 720
 CAGGTGGATC CCATGKTCT TCAGTAGACA AGTCACCTTT GTAGCTAGCA CCAGTGCCAG 780
 15 CTCCATGCCA TTGCACCTTC TTTAGTCTTG ATTGCCCTTC CCGCATTTWT TGGTGTATTA 840
 AAATGACTRA TKAAGCTAAT TAAAAGAAGC ATTCAAATCT GCTTTCTACC CTCATTAACA 900
 ATTAGCAGGG CACTGGCCAG AGTTTGTACC CTGTGTTTTC CCTTAACAAC ATTCTATTTC 960
 20 CTCTTTGTAT ATTAAAGTGT TGTAAAGAAA CGTGTTCCTA TCAAACTGA CCATGAGATA 1020
 AAGGAAAGAG ATGTGGCTTT TGTGATATTC TATCACAAC ACTTATTGTA TCTCTGTAAA 1080
 25 ATACAATGTA TGTATGCATG TAAGTGTTCCT TGTCTTAATG TTGCTACTCC CATGGCAAAG 1140
 AAAAAAAAAA GAATGAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA CTCGAGGGGG 1200
 GGCCCGTACC CAATCGCCCT 1220
 30

(2) INFORMATION FOR SEQ ID NO: 12:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1939 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 40 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

45 GAACACAAAC ATGCAGTCTG TAGCAGATGG TAATAGGCTG AYATATTACA CTGTGTGATG 60
 TAAATCTGAT AGGTTTCTTT CTCTCCAAGG ACAGCTTTTT AAATATTTAA CAGTATCAAT 120
 AATTTTTCAG TTTCTGTGAG AATTTTATAA TTTATAATTT GCAGACTTAA TGTATAATCT 180
 50 ATTTGTCTCT AACAATTACA AATATATTTT TTATTTTCAGA TTTTATATAT TCCTACCAGA 240
 TGGAGATAAT TACAGCTTTA AAAATTTTTC TTTTTCATT TTATTTTCACA CATTGACATT 300
 AAATTTTAT GGACACATAA TAACTGTACA TATATATGGG GTAGAATGTG ATGTTTAAAT 360
 55 ACATGTACTC AATGTGTAAT GATCAAATCA GGGTAATTTG CATAATGATT TTTCTGTAGG 420
 GAGAAAATTC AAAATCTACT CTTCTGGCTA TTTTCAAATA TATAATATGT TATTGTAAAC 480
 60 TATACTCATC CTAATATGCA ATAGGACACC AGAATTATT CCTGGGTTCT ACATCCGTTA 540

AGGCAACCAA GGATTGGAAA TATTGGAAAA AAAAATTGCG TCTGTAAGTA ACATGTACAG 600
 ACTTTTTTCT TGTCTTATT CTTTACACAA TATAGTACAA TAACTATTG CATGACAT 660
 5 ACATCGGATA TTATGAGTGA TCTAGAGTGT ATATGAAGTA TATGGGAGGA TGTGCAAGG 720
 TGATGTGCAA ATACTATGTC ATTTTATATC AGGGACTTGA GTATCCTTTG TTAYCCTCAG 780
 10 GAGATCCTGA AACYAGTCCC CCATGGATAC TGAGGGCTGA CTGTATAGTC CTATCCTCAC 840
 GGAACCTTCA TTCTAATGRG GGAAGACTGA CTATAACAA AATATATGTA ATAGGTGGTG 900
 GTAAGTACCG TGGAGAAGTA ACAAATGGGG CAAAGTGAGT TATACAGCTC CATYCTTAGA 960
 15 AACCTTGGAG TACTTTTCTT AGTTTATACT CGTGGTGGTT TCCTTTTGTC TCCTTTATTA 1020
 CATGGGACTC TGACATGTGC CCATAGCTAG GGTGGCAGTA GGATCTACCC GAAAAGCGTC 1080
 20 CTGCTGATAC AGGACCAAAG CATCCTGTTG TTCTCGAGCC TATAAAAAGA GCTAATGGTC 1140
 TTGCTTCTCT TAACTGTGGC CTCCTACACT GTGTTTGGGA TGATTGGTGA TGTCTTGGAT 1200
 ATTCTGTTTC TTTGGAACCT TGAATATACA ACACCTTACT AGGGAATTAG CAATGGAAGC 1260
 25 AGAGCAAAGA TGTACAGAGG AAACAATGCR TAACTCTGAT GGAATGAAG TCATGAGGCA 1320
 GCAGAGAGCT TAAATTASAG CTTTAAAAAT TTTTATTTT TAGAGGGAAT TTAMTTGGGA 1380
 30 GTAACAGCAG TAATAGTTAA CGGAGCCAGA ATGCTTGAGT CATATAATTG CAAAGCAGAG 1440
 TTGGGAGCAA CAGATGCTAA AGAGTAGTTG CTGTAGTTCC TCTTTGGGTC GTAGGAGCAG 1500
 TTGTCATRTT MCTATAYAGC TACTGCATGA AGAAGAGTTC TTAGTGAGGC CTGGGTGAAC 1560
 35 AGCTCTTCTT AGTATTCTGT GTGACCCCAT TYGACCTTTT AACAAATCCC TAAGTAAATA 1620
 AATAGCCCTT MAGGWAACT AAGTTTTTCT CTGCTGTTTT TTGCTTGAG AGAGCTATAA 1680
 40 CTGTAATAGA CTTATATTTC TGAACATTTT AGTGCTTGCC AATATTGGT AATATTATG 1740
 TTTCTATAT TTGTAATGAA CATTCTTCTT CMGGTACATT TYTTGTTAAA TTATTGTTTS 1800
 ATGSATAAAA GTTCACCTTT TATTGTATAA AATTGACTCA GATTAATTTA TACACATTGA 1860
 45 CAATGGGTAA ATAGAGTTTT TCAGATTATT AAAAGCTGAA GGATGCCCAT GTAAGCAAAA 1920
 AAAAAAAAAA AAAACTCGA 1939

50

(2) INFORMATION FOR SEQ ID NO: 13:

55

(1) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2602 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

| | | |
|----|--|------|
| | GGGTCTTCG GCGAACTTTC CTTTCGGGT GTTCTGAAGC GGTTTTCCTG TAATCCTCAG | 60 |
| 5 | TGAGGAAACC CACCGTGAAT CGGATTGCCG TTCAGTCCCA CGGAGGCCG GCTCGTGGC | 120 |
| | CATGTNGGGG ACGCATGTTC ATTAAGTTCA TTAAAATAAT TTCATTGTG TC GTTTGAA | 180 |
| | GACTGCTTCA TTCTGCCTCT AGTACCAGCG GTTCTCTGT TCTGTGATCA ATGTGATTCA | 240 |
| 10 | CAGGAACTCC TTAAGTAACA AACGAAATGA GCCAGGGGCG TGGAAATAT GACTTCTATA | 300 |
| | TTGGTCTGGG ATTGGCTATG AGCTCCAGCA TTTTCATTGG AGGAAGTTTC ATTTTGAAAA | 360 |
| 15 | AAAAGGCCCT CCTTCGACTT GCCAGGAAAG GCTCTATGAG AGCAGGTCAA GGTGCCCATG | 420 |
| | CATATCTTAA GGAATGGTTG TGGTGGGCTG GACTGCTGTC AATGGGAGCT GGTGAGGTGG | 480 |
| | CCAACCTCGC TGGGTATGCG TTGCAACAG CCACTCTAGT GACTCCACTA GGAGCTCTCA | 540 |
| 20 | GCGTGCTAGT AAGTGCCATT CTTTCTTCAT ACTTTCTCAA TGAAAGACTT AATCTTCATG | 600 |
| | GGAAAATTGG GTGTTTGCTA AGTATTCTAG GATCTACAGT TATGGTCATT CATGCTCCAA | 660 |
| 25 | AGGAAGAGGA GATTGAGACT TTAAATGAAA TGTCTCACA GCTAGGTGAT CCAGGTTTGT | 720 |
| | TGGTCTTTGC AACCCCTGTG GTCATTGTGG CCTTGATATT AATCTTCGTG GTGGGTCCTC | 780 |
| | GCCATGGACA GACAAACATT CTTGTGTACA TAACAATCTG CTCTGTAATC GGCGGTTTT | 840 |
| 30 | CAGTCTCCTG TGGAAGGGC CTGGGCATTG CTATCAAGGA GCTGTTTGCA GGAAGCCTG | 900 |
| | TGCTGCGGCA TCCCTGGCT TGGATTCTGC TGCTGAGCCT CATCGTCTGT GTGAGCACAC | 960 |
| 35 | AGATTAATTA CCTAAATAGG GCCCTGGATA TATTCAACAC TTCCATTGTG ACTCCAATAT | 1020 |
| | ATTATGTATT CTTTACAACA TCAGTTTAA CTTGTTGAGC TATTCTTTTT AAGGAGTGGC | 1080 |
| | AAGATATGCC TGTGACGAT GTCATTGGTA CTTTGAGTGG CTTCTTTACA ATCATTGTGG | 1140 |
| 40 | GGATATCTTT GTTGCATGCC TTTAAAGACG TCAGCTTTAG TCTAGCAAGT CTGCCTGTGT | 1200 |
| | CTTTTCGAAA AGACGAGAAA GCAATGAATG GCAATCTCTC TAATATGTAT GAAGTTCTTA | 1260 |
| 45 | ATAATAATGA AGAAAGCTTA ACCTGTGGAA TCGAACAACA CACTGGTGAA AATGTCTCCC | 1320 |
| | GAAGAAATGG AAATCTGACA GCTTTTAAAG AAAGGTGTAA TTAAGGTTA ATCTGTGATT | 1380 |
| | GTTATGAAGT GAATTTGAAT ATCATCAGAA TGTGTCTGAA AAAACATTGT CCTCAAATAA | 1440 |
| 50 | TGTTCTTTAA AGGCAATCTT TTTAAAGATT TCACTAATTT GGACCAAGAA ATTACTTTTC | 1500 |
| | TTGTATTTAA ACAACAATG GTAGCTCACT AAAATGACCT CAGCACATGA CGATTCTTAT | 1560 |
| 55 | TAACATTTTA TTGTTGTAGA AGTATTTTAC ATTTTCATCC CTTCTCCAAA AGCCGAATGC | 1620 |
| | ACTAATGACA GTTTTAAAGTC TATGAAAATG CTTTATTTTT TCATTGGTGA TGAAAGTCTG | 1680 |
| 60 | AAATGTGCAT TTGTCATCCC CACTCCATCA ATCCCTGACC ATGTAAGGCT TTTTATTTTT | 1740 |

| | | |
|----|---|------|
| | AAAAAACAG AGTTATCCCA ATACATTATC CTGTGATTTA CCTTACCTAC AAAAGTGGCT | 1800 |
| | CCTGTTTGTT TGATGATGAT TGGTTTATTT TTTGAAATAT TTATTAAGGG AAAACTAAGT | 1860 |
| 5 | TACTGAATGA AGGAACCTCT TTCTTACAAA ACAAAAAAAA GGGCAGAAAT CACCCCAGG | 1920 |
| | AACGATTTCT CAGGTTGAGA TGATCACCGT GAATCGGGCT TCCTCTGAGC ATTCGATGGC | 1980 |
| 10 | CTTAGCACCT CATCAAGCCA GCACATCCTG CCTGCTGTTG CAGCCTGGCT GGGTTTATTC | 2040 |
| | TTCACTTACC CTAATCCCAT GATGCCTGGA ACCTTGATTA CCGTTTACCA TCAGCTCTTG | 2100 |
| | TACTTTTCAG TATATTTTCA TAATGAGTTA TATTGTCAAT TAGACTTTGA ACAGCTCTGG | 2160 |
| 15 | GAAATAGAAG ACTAGGGTTG TTTCTTAAAT TTAGCTCATG TTATAATAAA AAGTTGAAAT | 2220 |
| | GAAGTICTTA TTCTAAAAGT CTGAATGCTT AGAACAACT TAACATGTTT ATAGAATATG | 2280 |
| 20 | GTCTCTTTGT ACCAAGTACT TTGCTTAAGA GCTCCTTTGG GCCACTACAT ATTTTGGTTT | 2340 |
| | CTAGAAAATG TTTGTTTATG AAGAAGTCGA TGGAAACTG CAAACATATG CAGAAAAGGT | 2400 |
| | AGAATAATAA AAAAGGTCTA ATGAACCTCA TTCAGCTTTG AACCTATCCA CTCATAACCA | 2460 |
| 25 | TTGACTGGCC TTTTAAAAA AAGTATTGGG CAGAATTAAA TTTCCACCTA GGTGATGGG | 2520 |
| | AAGGAAAGTG TTCGCCTGTN CCAGCCTGTG GTTCCTGCCT GGGNGGTTA CCCAGTGGTG | 2580 |
| 30 | GCGCCAGGCC AAGGTCCATT CA | 2602 |

(2) INFORMATION FOR SEQ ID NO: 14:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 808 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

| | | |
|----|---|-----|
| | ACCCACGCGT CCGGTAAAC AAAGGAATG ACGATATGGG AAAGAAAATA CATTTGGATG | 60 |
| 45 | TTACAGATAT GTGTGTTCTT GGAGCCAGG GCCAAGCCCT CCCTGGGGGA CTTGGATTGG | 120 |
| | TGATCTCTCT CCTTGGCCCC AACCTGACAT CTTTCTTGT CTTTGTAGGA ATGTCTGATG | 180 |
| 50 | GAAATTCCTC CTAACCTGGG GTCATACTCC ATTTCAATCT CTGGGCTCAN TGAGAAGGAA | 240 |
| | AATTTTCTTT TAAGTAATTT ACTGAAAACC CAGATCACAC CATCATAAAT TCAGATAGGT | 300 |
| 55 | GCAATCTGTC CCACAATGAA GGCAAAGTGT TACACTAATT TGAAAACAGT TTAGCCTCTT | 360 |
| | ATTCGCCCAA ACTTCATTCT TGAATTTTGT CATTTTGTGT GGGCAAGCTG TGGGAAAGGG | 420 |
| | GCACAAAAGT ATCACTGAAG TATTTTTCCT AAAAAGAAAA AAGGCAGTCT TCCTCTACTA | 480 |
| 60 | ATGAGAATGC AAAATGTTGA ACAACTGTAA AATGTTTCTA CCCTGCTTTT AGACATAAAG | 540 |

CTTTAAAAA CTGTGAGGTC TTTTATCACT TCCCCATGT ATATGTAATA TGGCTCCAGA 600
TAATTACTCT GCCACGGGA GAAAATCTTC CATAACTCTC CCCTATATAT ATGTATACTC 660
5 CACCACCTTA TCTTGTATG TCATGGTGGT GGGAGTATTT ATMCCACAGA AACAGGCCAA 720
TGATACAAAC CTGGGCGACA GAGCAAGACT CCACTTCAAA AAAAAAAAAA AAAAAAAAAA 780
10 AAAAAAAAAA AAAAAAAAAA GGGCGGCC 808

15 (2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 864 base pairs
(B) TYPE: nucleic acid
20 (C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

25 GGGTTTTTTG TTTTGTGTTT TTNAGGGGGG AGGGGGGGTT TCCCCTCCTT TGCCCCAGAC 60
TTCTCTTTGA ACACAAATGC ATTAGCCTTG TGGCTAGAAM ACCCTCTTCC TACCTCTGTC 120
TCCCCTCACT TGTCATATGC TCTGACATGC TAACATTCTT TTTGTTTCATC CCTGTTGCC 180
30 CCACAGAAAC ATCCCAGAAA AACCGGTCAG GTTTCCTTCC TCCCTGATCC TTAGGTTTCT 240
GAAATAGGGT TCTGTTACAT CCTCTTCGAT AGCCTGTTTA AAATGTTTAG AAGGCTGGA 300
35 GCTCAAAAAT GCGTTCCTCC ACATTGATAA TTTAGTAAAC TGAGAACATT GACATCACTA 360
CAGGGCAGCA TAAGAGGTTG CTTACATGTG GTAGCAGCTC TGGTTTGATT CAAGTTGCTA 420
CCATGTACAT TGACAGCACA TATACCATAA CCAGCGTGTT GGGTTGAATT GCACTTTCTA 480
40 CCTTTGTATG AGATTACAG ACTTTCCTTC TGGGTTTGTA TCATGACCAG AGGGGTACTA 540
TAGGGTTGGT TTATACTGCA ATATAGAGGA TCAGAAGCCA TTTGATTGTT TAGGTGTGTC 600
45 AGAAGGGAGA ATGATGGCAG ACGAACTGCT GGAAGAGGTC AGAAGATAGC CATGCTAAAA 660
TGCAATTATA TCCTCATGTT TATCCCAAAC TAATCTTGA CTTTCCACT CATTAGCTTT 720
GTTTGCCTT TGTTCCTT GAAGGTTTAA GTTCAACCAT ATTCTGTCAA CTGTTCAATT 780
50 TCAGTGGAAT CTTGTATTTC TGGTTCATTA TAACAAATTG TTCGCTTAAA AAAAAAAAAA 840
AAAAGGGGCG GCCGCTCTAG AGGG 864

55

(2) INFORMATION FOR SEQ ID NO: 16:

60 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2361 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

| | | |
|----|---|------|
| | GGCACGAGCT CGAGTTTTTT TTTTTTTTTT TTCTATTTT TGCCAGACTC TTGATACTCT | 60 |
| 10 | TAAAACTTGT TTGTGGTCAG CACAACAAGG AACAAAACAA AGCTTTGAAA AAACCTTAAC | 120 |
| | ATGAAAAAAC GCACTGACAT TTTTTTTTAT TTAATATAGC CTGGACTTTA CCTGCGTATG | 180 |
| | CACATGCTCA GAATTGTCTA CTAGGCTGAC TATGTATCAC CTCTTCAGCT TGGATCCAAT | 240 |
| 15 | TGTGGATTTA TTACAAACA TCAAATGCCT TCAAGCCAAT CCTTTTGTCT GTATGTTTGT | 300 |
| | CAGCCTACTG TAGTAGATAC GCAACAGATA WTGTGGGAAA AAAAGAGATA AGAGGAGGAA | 360 |
| 20 | GCTAATAAGA GACTGTCAAG ATTGTATACC TTCTTGGTTT CTTTAAAGAA TTTGTTGCCT | 420 |
| | TTCTACTATT ACAGCAAAGC AGCATTTTGT TACTGACTGC CTAAAATCAC TTAATCTCAG | 480 |
| | GTGAACGCAT CACTTGCCAA ACTGTGGAA TGCTATTGTG GTTTGTGTGC ACTGTTTTTT | 540 |
| 25 | TCGTTTGTGT GTTTGTTTAT TTGGTTGGCT TTTTGGAGAG GGAAATTGG AAACGGGACA | 600 |
| | TACACAAAAG TTACACACCC ACATTCCCTT TTTATCATGA CATACAAGAA GAAACTAGCA | 660 |
| 30 | GAGCTAAGAA TGGAGTGAAG AAAGGCAGTA TGGCAGGCAC CAGCAAAGAG TTGAGGGCTG | 720 |
| | TTGCTCTTAA AAATTATTTT TTTTATTATT ATTTTGAAAG TATGGAAGTT TTCCATTAC | 780 |
| | TGGGGAAAGG AGGGAAAAGT GCATTTATTT TTATACAGAG TTACTTAATT ACCTCCAAAA | 840 |
| 35 | CACATATGTT GGAAATCGCT TTTGCTGGTG CAAAGTATAT TAATGAGCAG GAATACATAC | 900 |
| | ATTGAGGTTA TGAATAGAGA GCTCAATTTG TACCTTTGCT GTCTTGCTCA AGCTTGGTAT | 960 |
| 40 | GGCATGAAAA CTCGACTTTA TTCCAAAAGT AACTTCAAAA TTTAAAATAC TAGAACGTTT | 1020 |
| | GCTGCGATAA ATCTTTTGGG TTTTGTGTTT TTTCTAATGA GAATACTGTT TTTCAATACC | 1080 |
| | TAAAGAACAA TTGCTAAAC ATGAGAAATC ACTCACTTTG ATTATGTATA GATTACATAG | 1140 |
| 45 | GAAGAACAAT CACATCAGTA AGTTATAGTT TATATTAAAG GTAATTTTCT GTTGGCTCAT | 1200 |
| | AACAAATATA CCAGCATTC A TAGATGATT TCAGCATTTT CCAAGGTACC AAGTGACTTT | 1260 |
| 50 | ATTTTGTGTG TGTGTGTGTT GTGTATTTT AGAAGGAATT CAGCTCTGAT GTTTTAAAG | 1320 |
| | AAAACGACGA TCTCTGATGT TGCAACATAC GTGTAAATG GGTGTTACAT CTATCCTGCC | 1380 |
| | ATTTAACCCC ACAGTTAATA AAGTGGCTGA AAATAATAGT AGCTCTGGCT TGGTGCTTGA | 1440 |
| 55 | CCTGGTTAAA TACTGTCTTA AAGCTCATAA AAAACAAATA GGCTTTTCCA TAAGTGGCCT | 1500 |
| | TTAAGAAAAC ATGGAAGACA ATTCATGTTT GACAAATGCT GACAGGGTGA AGAAAGCCCA | 1560 |
| 60 | GTGTAAAAAT GAATCGCGTT TTAAGTGATT CGGTAAAGA GTTTGGGCTC CCGTAGCAAA | 1620 |

| | | |
|----|---|------|
| | CTAATACTAG TAATAAGGA AATGGGGTG AAATATTTT TTATGTTGA ATCATTTTGT | 1680 |
| 5 | GAATGTCCCC CTCAAAAAA GCTAATGGAA TATTGGCAT AAAGGCCATT TGGTGGTTT | 1740 |
| | ATTTTGT TTTT GAGGGGGWTT GTCAGAAAAT CCCTTTTCTC TCTTACGYCT AACTGACTAG | 1800 |
| | GGAACAATTG TTGATATGCA TAGCATTGGG AATACTTGTC ATTATATACT CTTACAAATA | 1860 |
| 10 | ACACATGAAG CAAGAATGAC CAATATTCTG NATAATTGGG CACTGGGATC ACAAATGTG | 1920 |
| | ATAAACTTTT AAATGTATAA AACTTTATCA AATAAAGTTT TATTTTCCCC TTAAAAATGT | 1980 |
| 15 | ATTTCTTTAG AGGCATTACT TTTTAAAAA TATTGGTCAA TTCCTGACAT AAGATGTGAG | 2040 |
| | GTTTACAGTT GTATTCCAGT ATTCAAGATA GATTCTGAT TTTTCAATTA GGAAAAGTAA | 2100 |
| | AATCCAAAAT GTTAGCAAAA CAAAGTGCAA TATTAAATGT TTGCTTTATA GATTATATTC | 2160 |
| 20 | TATGGCTGTT TGTAAATTCT CTTTTTTCC TTTTATTTT GGTGCTGAAT ATGTCCTTGT | 2220 |
| | AGGCTCTGTT TTAAGAAAAC AATATGTGGG AAATGATTTA ATTTTTCCTA TTGCTCTTCC | 2280 |
| 25 | TTGTGAAAA TAAAGTGT TGTTTTTTTC TGTTTGTAA AAAAAAAAAA AAAAAAAAAA | 2340 |
| | AAAAAAAAA AAGAANGAGA A | 2361 |

30

(2) INFORMATION FOR SEQ ID NO: 17:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 803 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

35

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

| | | |
|----|---|-----|
| | CAGCTGCCCA CAAGGTGGC TCCTGGGGA GGGTCATCCC TCTGAGAAGA GGGCGGCACC | 60 |
| | AAGACCCACA CACCTGAAAA ATGTGGTACT TCATGTCGCT GATCTCGATG GTCTTGCTGC | 120 |
| 45 | TGTCCCCATC CTGTTCTGAT TTATGGTCA TTAGTGTCTT GAACCTGGAG CAAAGGAGAC | 180 |
| | AAAGCAAGGT GGGTTTGA CTTTACTT CACCACTGTG TGGCGNATGG CACCATCTGT | 240 |
| 50 | CACCTGACCG GCTACCACAA GACGAACAT TTAAAAATT ACTGCTGTGC TCCTAAAATA | 300 |
| | ATTTTCAGCA AGTGCCATTT TACACCATCT TAGGAAGACA TCTGAGCTGA GCCCAATTCT | 360 |
| | GTCCCCACCA CCCACCTAC AAGCGACCTG ACGCCTGTGG CCAGAATGCT GACTCTTCAT | 420 |
| 55 | TCCAGGATAT TTATGTTTTC TAATAATAAA AGCAATAACT AGGCCAGAAA GAACACCACC | 480 |
| | TCAGAGCCCC CCTTCTCTGC TGCCCTGGGT CCACCCCGTC TCATCCCGCT GTGGGCGGAG | 540 |
| 60 | TGGGCTCTG CTGCAATGTG ACTGCAGTCT GAGGGGCAGA RGCTGCAGGK TACAGCCCCA | 600 |

GCGAKTCACT CTCTGTCACC TGAATCTGA AACAAAGTGC TTCTGTGCCC CTGGGCTGGG 660
AGTTTGTAT CTGAGGCTGC CT, CCTGTTA GAACNTGTCA CCAGCAGGAC TTTATGTGCA 720
5 TAAACAGCT TTCCTTCCAC CAAAAAAAAA AAAAAAAAAAC TCGAGGGGGG GCCCGGTACC 780
CAATTCGCC TATAGTGAGC GAT 803

10

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:
15 (A) LENGTH: 1794 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

TTCTTTTITG TTCATGGGAC ATGGTACCTA AGCAAATAGG AGTTGGGTTT GGTITTTTCTC 60
CTAAAATAAT GCTCAATACT TACCTAATCA AATGGCATCC ATTGAATAA AATGACAATA 120
25 ACTAAAGCTA GTTAATGTCA GTGACATTA ACTAACTCCA GGATTCAGGA GTTTTAATGT 180
TAGAATTTAG ATTTAACAGA TAGAGTGTGG CTTTATTGT CCATGGTAGC CCATCTCTCC 240
30 TAAGACCTTT TCTAGTCTGT CTTCTGCCT TCGAACTTGA TGACAGTAAA ACCCTGTTTA 300
GTATCTCTT GTGCATTGG TTTGTGGTT AGCCGACTGT CTTGAACTA TTCATTTTGC 360
TTCTAGTTTT ATTTACAGA GGTAGCATG GTGGGTTTT TTTTTTTTT CTGCTCTGT 420
35 GTTTGAAGTT TCAGTTTCTG TTTTCTAGT AAGGCTTAT TTTGATTAGC AGTCAATGGC 480
AAAGAAAAAG TAAATCAAAG ATGACTTCTT TTCAAATGT ATTGTTTAGC ACTTAACTCA 540
40 GATGAATTTA TAAATTATTA ATCTTGATAC TAAGGATTG TTAATTTTT GCATATTAGG 600
TTAATTTTTA CCTTACATGT GAGAGTCTTA CCACTAAGCC ATTCTGTCTC TGTACTGTTG 660
GGAAGTTTTG GAAACCCCTG CCAGTGATCT GGTGATGATC TGATGATTTA TTTAAAGAGC 720
45 CGTTGATGCC TCCAGGAAAC TTAAGTATTT TATTAATATA TATATAGGAA TTTTTTTTTA 780
TTTTGCTTTG TCTTCTCTC CCTTCTTTA TCCTCATGTT CATCTTTCAA ACCAGTGTTT 840
50 TGAAGTATG CATGCAGGCC TATAAATGAA AAACACAATT CTTTATGTT ATAGCATGTG 900
TATTAATGTC TAACTACATA CGCAAAACT TCCTTTACAG AGGTTGCGAC TAACATTTCA 960
CATGCACATT TCAAAACAAG ATGTGTCATG AAAACAGCCC CTTTACCTGC CAAGACAAGC 1020
55 AGGGCTATAT TTCAGTGACA GCTGATATTT GTTTTGAAAG TGAATCTCAT AATATATATA 1080
TGTATTACAC ATTATTATGA CTAGAAGTAT GTAAGAAATG ATCAGAACAA AAGAAAATTT 1140
60 CTATTTTCAT GCAAATATTT TTCATCAGTC ATCACTCTCA AATATAAATT AAAATATAAC 1200

ACTCCTGAAT GCCTGAGGCA CGATCTGGAT TTTAAATGTG TGGTATTCAT TGAAAAGAAG 1260
CTCTCCACCC ACTTGGTATT TCAAGAAAAT TTAAAACGAT CCCAAGGAAA GATGATTTGT 1320
5 ATGTTAAAGT GACTGCACAA GTAAAAGTCC AATGTTGTGT GCATGAAAAG GATTCCTTGG 1380
TTATGTGCAG GGAATCATCT CACATGCTGT TTTTCCTATT TGGTTTGAGA AACAGGCTGA 1440
10 CACTATTCTC TTTGATTAGA AAATAAACTC ATAAAACTCA TAATGTTGAT ATAATCAAGA 1500
TGTAACCACT ATAAATATGT AGAAGAGGAA GTTTTAAAAG ACCTTAAGCT GGCATTGTGA 1560
AGGAACACCA TGGTAGACTC TTTTGTAAA TGTATTTTGT ATTTAATGAA ATGCAGTATA 1620
15 AAGGTTGGTG AAGTGTAATA TAATGTGTGA AACAAATCCT GTTAATAGAG AGATGTACAG 1680
AATCGTTTGT TACTGTATCT TGAAACTTGT GAAATAAAGA TTCCACCTCT GGTAAAAA 1740
20 AAAAAAAAAA AAYTCGGGGC CAGTCCCCC CCGGCTATTT TAAAGGNAA AAAG 1794

25 (2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 1037 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

35 TCGAGTTTTT TTTTTTTTTT TGACAGAGTC TTGCTATGTT GCCCAGGCTG GAGTGCAGTG 60
GCAATCTTGG CTCAYTGCAA CCTYTGCTC CTGGGTCAA GCAATTYTCC TGCYTCAGCY 120
TCCYTAGTAG CTGGGACTAC AGGCACCTGC CACCATGCCA GGTAACTTT TTGTATTTTA 180
40 GTAGAGACAG AGTTTCACCA TGTGCCCCAC GCTGGTGTG AACTCCTGAG CTCAGGCAAT 240
CTGCCACCT TGGCCTCCGA AAGTGCTAGG ATTACAGGCT TGAGCCACTG CACCCAGCCA 300
45 AGCTGTACTT TTTTTTTTTT TTTTAAAGCT TCAAACCTC AATATTTTAT TAAGAGTTAC 360
AGTTTGGTTT CAGTCATTCK GAGGRAAATT AAGGAAGGG CTGGCCCAW ACCTGGTAAA 420
AGAATGGAAG GAACCAATTT TTAACCATTT GGACCACTGA TTYTCAATGG GAGTGCTTTT 480
50 TGTCCCCCAG GAAACATCTR GAAAGGTATA WKGAGATATT TSTGGSTTGT CACAATTTGT 540
GATGGGGGAA AAAAGAACTA CCAGTATCAG GGGGATACAG GCCCGGTATC AGGTGGATAG 600
55 AGGCCTGGAA TATTGCTAAA CATCTACAG TGCAAAGACA SCCTTTMACA WACAGAACTA 660
TYTGGTCCAA AATGTCAATA GTGCTGAGGT TGAAGAACTC AATATTTTAT ATGTTTTCAG 720
GGAATTTCTA TGTGGGCTTG GGAAAGTTG AAGTCAATTG TCATTTGTAT ATTTAAAGGG 780
60

ATATATTTTA TCATTAGTCT ATAAATTCCA GTTGCAAAGT AGAGGCCCTG CACATTGTG 840
 CACATATACA CACACCAGAA ATAAAYTMTG TKGCAATTAT CTTCTC ATC ATTGACAGGG 900
 5 CAATGACCTA TGAAAATTAT GTTATGTCTA ATAGTCCCTC ATTGTTATGT GCAAAACACC 960
 CAGCAAAGCT CAAGTTAAGR TTGTGGTCAC AAAGAAAAGA GCTATCATTG CTTTATGATG 1020
 TTGTCTGAAG TTAATGA 1037
 10

(2) INFORMATION FOR SEQ ID NO: 20:

15

(i) SEQUENCE CHARACTERISTICS:

20

- (A) LENGTH: 1309 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

GGCACAGACT TTAAGAAATG CCAAATGCAA GGACCATTAA GAAATTTCTC CCCGAAATGA 60
 25 GGCTCCTCTA ACAAATGATG ATTANAACGC TCTCTCCTTG AGCAGTCACA TTCTAGAAAC 120
 ACGACATTCC ATGAGGCAGG AAGAGTTCAG TTAATTTGCT CCKGAAAAAG TGTGGTTCAG 180
 30 TGTMTGTGTG GCAATGTACG TGGGCAGAAG AGGCCGCTCA AGCTGTGTCC CCCCTGAGCA 240
 GGATTGAGGA AAGGGAAAAG AAGTTCTCTT CAACTCAGCC AAGGGGCCGT ACGATGGCCG 300
 ATGAGATTAT GTATTTAAAA GTTCTTTGTA AAGTGTAAAC TAAAAACCTT AAATGTAAGA 360
 35 TGCTGTTGTT ATTATTACTG TTGTTGTTGC TGTATGGAC ATGCCAAAAG GCCCTTGTTA 420
 GAAGACAGTT TTGCCTTTTC AATCTCATAG CAAGGAACTC AAGTCTGATG CTTCAAAAAG 480
 40 ATGAGAAGAA GGGCAAGAAG AGGGATAACT CCCAAGCTCA GAGGGAAAAA AAAGGTGGGG 540
 GAAAAGAGCC CCAGGGTGAC CTTGAGGAAA GGCCAGGACC AGGATGATCT AACCTTTCCC 600
 TTCACCAGAA ACAAAGCTAT TGCCAGACTG AACCTTAAAG TCAAGCAGTC ACCCACTGCC 660
 45 TTTGCTGGGA GCAGAAGCCC ATAGCAACAA GTGACCTGCC CCTCAGACTC AAGATCCCAG 720
 ATACCAGAGC TGGAGGAGTC ATAGGGCATT ACTGGTAGGC AGGAAAACCTG AGGGTCGAAC 780
 50 AAATGGAAGA ATGCGGTGAT CATAGACCAA AGACACACAG ATAATTAACC CCATGTGTCC 840
 ACCCAGGCCA AAGTTCTTCC TGCTACCCCA CAGTGGATGT CCAGGCAGAT GGTCCCCACA 900
 TGATGGGGAA GCAGAGGGCA TAGTGTGGTT TTGTGGGACT GTTTCATGTT TTGTAGTGTG 960
 55 GGCTCAACAG TGCCAAAGGA AACACTAGGG AAAAGTTGGT GAAACATGCC AGCTAGCAGG 1020
 ACCAGTAAAG GCATAATCAG GCATTTGGCA AAGCTTGCTT TTCTAATTCA ATGATAGGTT 1080
 60 CTAATAGGAA ATTTTGAAG ATTTTATAA ACAATGTTAT AGTGGCACTT CCCAGTATG 1140

GAATAAATAA CATGCATTCT TTTTCAATA TACTGTCATA TTCAGATGTC ATTAAATAA 1200
ATGGATGAGT CACAGAGGAG CTATCAGATG CTCTCATGAC TACCATAACT CAAAAAA.A 1260
5 AAAAAA.AWA AAAGGGGGC CCGTACCCAT TTGCCCTAAA GGGATCGTA 1309

10

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:
15 (A) LENGTH: 1081 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

ACANATNTTT TACTTAAAT TTATTTTATC TTATTTTATG GTGCTTTTAA TCTCAAAAT 60
CTGAAAGCG AATAGCAGT GTTTTCAGAA ACAATGTGA AAGCAGTCAA ATTAAGTAGA 120
25 TACTATTTAG AAATGTAAAA TACTCTCCAG ATCTACCATT AATAGAAAT AACTAAACC 180
TTATATTTTA TTTTGCCAA AATATTTTAT TATAAATAT GACCAAAATA TTTAAATGC 240
ACAATGCTTT TAACCTAAAT GTGCTAACCC TGTTCCTGTC TGTTTTGTGC TGTACCTTTT 300
30 CTGATTCMGA ATTATAGAAA ACTTGATAAA TACTTGATTT TAACCAATGA GACTACAGGC 360
AGATGGGACT AAGTGTTTAT GGGACAATTA TGTACTATTT AACTTAAATA TATTTTGTTT 420
35 AATAGGAAAT ATATAAAT AGCATTTTAT GTAATAAAT ATGGGCAACG ATTATCTTGG 480
AAATTAAAGA GTCAAAGCAA AGAAATGAAG GGCTGGTAAA ATGAATTTTG TAATATCCTC 540
AGGATACTTT TATCTTAAAA GTATGTTGTT AAAGATTTTG TAAATTGTAT TTCAACAATT 600
40 TTAAATGTGT TGAGCAAGTT GCAGTGCAAA CACTGTCATT ATGTAGAGAG TTTATATGCA 660
CATAATAACC TGTACCTATA AATCGTGCAA TAACCATATG CGACTATTTT GCCATGGAGA 720
45 AATCTGACAG CATGCAAAC AATAGTATTG TTTGATGTAG TTAACCTTAA GTTATTTTTC 780
AGTAATTTCT TCACAAATCA AGATTCAAAC AGCTTTAAAC ACTTCCAATG AGATAAATA 840
TTTACTATTA TGCTTATTAG AACAAAAGGT GTTTAAGGAT GAACTAAATA TTTTAATTGA 900
50 GCATTTATAT GGATAATCAT ACATTATGTA AGCCCATATG TATTTACATC CAGAGTCATA 960
ATATTTTAAA TAAACAATCA TGCAGAACT TTTTATAGGG GTATACTATT GTTTTAATAT 1020
55 CGTTGCCAAT TINGCTGACT TAAAATATGT GACATTTTAA AATCAGGATT TTCCATATTN 1080
G 1081

60

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 807 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

GAATTCGGCA CGAGCTCCTT CAGAAATGTC TTGGCTATTG TTGCTCTTTG CTCTTCTCTG 60
TAAATTTTAC AGAAGAGTTA 120
15 ATGTGTCTAA CTAGCAAACA CGAAGAAAAG CTCAGTGTTA GCAGTTAACT GAGGGAATGC 180
AAATCAAGAC CACAAGGAGA TAACAATTTG AGCCTATTGA CAAAAGTTCA GAAGTCTAAT 240
20 AATACTAAGT GTTGGAGAGG ATATGGCCCA GTATGATCTT ATCCACTGTT GGTGGGAGTA 300
TCAATTAGTA CAAACACTTT GAAAAATAAG ARGGAATTCT ATAATATCTA ACATTTGCAT 360
ATATCCATTT ATCTCTCTAG ATCTAGATCT TAGCCCTCTC CACCTGCAC TGTGTTCTTG 420
25 GAAGGGGATC ATGAATGGTT TCCTTGCAAT CTGCCTTCTG ATTTGGTTCA GCCAATGAGA 480
GACCATGGCA AGACATTTGT GAGAAGGGTA GAGAGTCAGG TCAAGGTTCT TAGTGAGATC 540
30 AACTCTTTCT CTGCCAGTTT GTTAACTGAA TTCTACTGAA AGCTAGAGCT CTGTTGAGTA 600
ATCTTTTAAA GCTGCAGCTA CCTTTTGAG ATTAAGTAAT AGCTCCCTGT TTGTGCCTTG 660
TTAGGGCTAG GGATGTTTAA GGATCCTTGC CCTTGCTAGT CCTAGCATGT TTTGTTGTCC 720
35 CATAATAGTT CTTTTTTTAA ACTTTCCTCA ATTACACAAT TTGATCTTGT TCCTACCAGT 780
ACCNITGCTG GTACAACCTT AAACCTGG 807
40

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 632 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

GAATTCGGCA CGAGTCTAAC AGCATAAAGA AATAACAGCT GCATTCAAGA CCAGGATATG 60
55 TAAATAAATT TGTTTAGTTT CAGCCACTTT TTAAAGTCAA TTTTACACCC TGAAAGAAAG 120
GCAATCTGA CTCCATTGTT CTTTCGCCAA TAAGGAGATC GGAATTTACA ATAATAAATA 180
GAAGAAAGAA TGTGCTTTT CCTCACTGTA ATTAATTTTA TGGCTCTTGC GAAGATGAAT 240
60

TTTTGTGGTG ATTAAATAG TCCCTTGAC ATATTAGGTA CTCAGTAAGC ATTTGTGAAA 300
 TAGGGACTTT CTAGCCTTTA TTTGTGTTA AGGAATCAGG GAATAAGTTC AAAATGCTT 360
 5 TTCAAGAAAT TTTTGGAAC CTCTTCTCAC TAAATAACTG TAAAGTCTTA TAAAGACAC 420
 ATTATTTATT TTCTCCAAGT ATTGCTTGCG AGGTGAATG AAGGTTTTTT TTTTATCAAC 480
 AGTTGTTTAA TAAGATCGTT TGAGGACTAA AAGGGCTGAT TGTAATCACC TGTAACATGT 540
 10 TACCCAGCAA GACATTCCTC ACCAGGTGA AGTAAAAAA ARAAATGAAG TGAGAATATC 600
 AAGCTTATGC AAGTTTGAAA TTNCAACAA GA 632

15

(2) INFORMATION FOR SEQ ID NO: 24:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1358 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

GGCACGAGGA TAAATTGCAA GTATTAATCG GTCCCAACTT TAATATGGGA TAAAAATAAC 60
 30 AGTCAGTATG TGACCTCCTA AACAATCCCT CTAAGTACTG GTGGAGGGGA GAAGGGAGGT 120
 CCTGGGGCCA GGACAGACAG GGCTATTTTC AGTAGTACAA CTTATATGCT ACTCTAAGAA 180
 AAGTCCAGAA AATGCRATTC TCTTCATACG AAGTCTTARA TACCCATCATK ATTTTGATAA 240
 35 ATACATTTTC ARRTCTAATA TGGAGACAGA AAGCTGCCTA GATTTATACC CACAAGTATT 300
 ATAAATTTAG AGAGTCTGAC CAGCCTCAAT TATTTCTCTT CGAAGTGGGA GAGAGAAATC 360
 40 AAAAGTCAGA AATGGTGGRT AATCTCCAAG TCATATCCAT TTGGSTTTGR TCTACTACTT 420
 GTTTTATATG TTGTATTTGG RGRCAAGRT GCCTGATGTT AAGGGRATTT CMTACMTTGA 480
 ATAATGTGAC CAGACTGCCA TCTAGTCAA AACCTATAAA ATGTTATTTA CTTTAATTCT 540
 45 GGGCTAATTC AACAGAAGTY YYSGATAAAA RCTCTCCAAA CAATAATTAT GARCCTTAGT 600
 TTTTGTTTTT GTTTTGATA CAAAACAAA CAGCTCTGTA GTTGTCTGT GAGGTTTATA 660
 50 AATAGATTTT TTAACTACT TAATTTTCYG GTTTCYGCCY CTGKGTTCYC TGTACCTATA 720
 GAGGTAGCTC TTTTCAGTTA AGTAGAGAAA AGCTCTTCCC CTGGGTTGAA AATAATGCAG 780
 TCCCAGAGAG CTACTTAACT CTACCTTTCT GGAGGTCATG GTAGCAATTG GAGATCTCCC 840
 55 AGGCATTCTA AGGGAGCTA CTAAAGAGCC CCAGATACTC AATTTACCAC TAGAAATTCG 900
 CTTCTCTAC TCTCTGTCAT CTGGGGAGRA AAGTATTATA ACTGACATTC AGTATGCACA 960
 60 CAATAAGTGC ATAATAAAGA GCTATTGAGG GGATCCAAGG GAGTAAATG GGTTTGCCCA 1020

5 TAGGACTCCA TCAGGGTCCA CCAACACAGA CTTACAGCAA AAATTGGAAG GCTCTTTTCT 1080
GCTGGATTCT GGAATCTGT GTTCTCTAGT GTGCCAGGA GAGTTGGAAT CAAAACACGT 1140
AATATAATGT TTCTATTTCAG AGCCCCATTT TTTTGCCAAA TAAAGTAGCA CTGTCAAATA 1200
ATAAATCTTG TATTCACCTG GGCATGTATG TTTATTATTG GATCTCTAAA ATATGCTTCA 1260
10 AATAATGCAC TGAAATAAGT GAGGTGATGA ATTTTGAAAT AATAACAGTT TATGATGGGT 1320
AGCTCCAAAA TTTTAAAAA AAAAAAAAAA AAACCTGA 1358

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(2) INFORMATION FOR SEQ ID NO: 25:

20 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1376 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

CCCACCTTTA GCGAGCCAAC GAGAGAACAC CGCCTGCAGC TAGAACAGCC TGGTCAGGAG 60
CGTAACGGAG TGGTGCGCCA ACGTGAGAGG AAACCCGTGC GCGGCTGCGC TTTCTGTCC 120
30 CCAAGCCGTT CTAGACGCGG GAAAAATGCT TTCTGAAAGC AGCTCCTTTT TGAAGGGTGT 180
GATGCTTGA AGCATTTTCT GTGCTTTGAT CACTATGCTA GGACACATTA GGATTGGTCA 240
35 TGGAATAGA ATGCACCACC ATGAGCATCA TCACCTACAA GCTCCTAACA AAGAAGATAT 300
CTTGAAATTC TCAGAGGATG AGCGCATGGA GCTCAGTAAG AGCTTTCGAG TATACTGTAT 360
TATCCTTGTA AAACCCAAAG ATGTGAGTCT TTGGGCTGCA GTAAAGGAGA CTTGGACCAA 420
40 ACACTGTGAC AAAGCAGAGT TCTTCAGTTC TGAAATGTT AAAGTGTTC AGTCAATTAA 480
TATGGACACA AATGACATGT GGTTAATGAT GAGAAAAGCT TACAAATACG CCTTTGAWAA 540
45 GTATAGAGAC CAATACAACCT GGTCTTCCT TGCACGCCCC ACTACGTTTG CTATCATTGA 600
AAACCTAAAG TATTTTTTGT TAAAAAGGA TCCATCACAG CCTTCTATC TAGGCCACAC 660
TATAAAATCT GGAGACCTTG AATATGTGGG TATGGAAGGA GGAATTGTCT TAAGTGTAGA 720
50 ATCAATGAAA AGACTTAACA GCCTTCTCAA TATCCCAGAA AAGTGTCTG AACAGGGAGG 780
GATGATTTGG AAGATATCTG AAGATAACA GCTAGCAGTT TGCCTGAAAT ATGCTGGAGT 840
55 ATTTGCAGAA AATGCAGAAG ATGCTGATGG AAAAGATGTA TTTAATACCA AATCTGTTGG 900
GCTTCTATT AAAGAGGCAA TGAATTATCA CCCCAACCAG GTAGTAGAAG GCTGTTGTTT 960
AGATATGGCT GTTACTTTTA ATGGACTGAC TCCAAATCAG ATGCATGTGA TGATGTATGG 1020
60

GGTATACCGC CTTAGGSCAT TTGGGCATAT TTTCAATGAT GCATTGGTTT TCTTACCTCC 1080
 AAATGGTTCT GACAATGACT GAGAAGTGGT AGAAAAGCGT GAATATGATC TTTGTATAGG 1140
 5 ACGTGTGTTG TCATTATTTG TAGTAGTAAC TACATATCCA ATACAGCGTG ATGTTTCTTT 1200
 TTCTTTTCTA ATTTGGTGGC ACTGGTATAA CCACACATTA AAGTCAGTAG TACATTTTTA 1260
 10 AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 1320
 AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAA 1376

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(2) INFORMATION FOR SEQ ID NO: 26:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 2923 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

25 CTCCTCTCC GGGGCCCCCT CCTCCCCCTT TMACTGGTGC AGATGGCCAG CCTGCTATAC 60
 CACCACCGCT TTCTGATACC ACCAAGCCCA AGTCCTCCTT GCCTGCCGTG AGCGATGCCC 120
 30 GTAGCGACCT GCTTTCAGCC ATCCGTCAAG GTTTTCAGCT GCGCAGGGTT GAKGAGCAGC 180
 GGAACAAGA GAAGCGGAT GTGTGGGCA ATGACGTGGC CACCATCTTG TCTCGTCGCA 240
 TTGCTGTGA GTACAGTGAC TCAGAAGATG ACTCCTCTGA ATTTGATGAG GACGACTGGT 300
 35 CCGATTAACT CTTTCTCGCT GCTGCCACC TTCTTTTCTT TTCCTTCCTA CTGCGCTTCT 360
 TTGATGCCAA CCCCACAGA CCGTAGGGG AGGAAAAGG AGGAAAAAG TAATTTTAAG 420
 40 GGGCCAAAGC TTTCCTGAA GCAACCAAAG ATATATCCAA GTGCTTCCTC CAAGTCAACA 480
 TGTATTTCTT CTCCCATTT TCAGGCCCTG TGGGCTCCT GAGGTTCACT AGCTGGGATG 540
 TTCCCTCTTT CTTCAAGTG CCTGTTGCAT ATTGAAAGGA AGGAGAAATC CCAAAGCAGA 600
 45 TTCTTTGAT CGGTTTCTG TTGGAGATGG GGCTTCCTT AGGAGCCATA TTCAACTACA 660
 GCCTTCTAAA ACCTGTGCCC TCAGCCACTT CGAATGCCAG CCACCTTCTG GTTCTAAAAC 720
 50 GGGGAGTGGT CTGAATGAAC ACAGCTGACC CCTTTCCCGC GCACTGAAAG GGCAGAGTAG 780
 GCCGAAGGTC CAAGGGCCAG ACTGCCTCAC CCTCTGCCCT AATCAGCAGG GTGGGCTGTC 840
 CTTTGTCTAA GCGATCTCTA TGCCTGGGAT GCCCTTTATT CCAGGAGGCA TCAAGCCTCT 900
 55 AAAGAATGTC TCACCTCCTC TGCCCAAAA TGATGCCTTT CTGTAGGCTG GTGTGTGTC 960
 CTCCCTCCCA GGATCCCTTT GGTGAGTATG GTGTTCAAGG TGCACCACCA CCACCTCTAG 1020
 60 ATACCTTCAG GCAACACAGC CCAGTTTAA CCTCTAGTAT CCATGACCAA ACTATCCCTG 1080

| | | |
|----|--|------|
| | ACACATGAGG ACAGGGGCTT CTTCTGGCTG TCAGGAGCAA AGCCTGAAGA CTGGAGCTG | 1140 |
| | CAGGACTGGA AGAACAGTGG AGCCCCGTGG GTCTCACCCT TTAAGGATGC TGAGGCCAG | 1200 |
| 5 | AGATGGGAAG TGACTTGCTC AAGGTCACAC AATTGGATAG TGACATAGCT AGAGCCAGA | 1260 |
| | GTTCCTGATT CCAAGTCACC TGTGCTTTCT GGGACCAAAG AATGGGCACC TGCTGGAGTC | 1320 |
| 10 | CGGGCAGAGC TTTCTCAGTT GTATTGCTAC TCCAGACCTC ACCATAGGTT GGGGTCCCAG | 1380 |
| | TAGGAAGGCT CAGGCTCTGT GCCAGCCCTG TCGGTGCTGC TCAGACCTTC ATAGCCTCTC | 1440 |
| 15 | TTGTCAATCT TTGTGCCCC TTTTCTGTCA CCAGCCAACC ACATAGCCTT GGGACCAGCC | 1500 |
| | TCTCTGGGG ACCAGAAGTA GTGAGAGAAG GAAGGGGATA GGCAGCTTTG ACAGGTGCTG | 1560 |
| | CTTTCAATTC CTCTCAACT CCTCCCCCTT TTATTTCCCC AATTTAAACA AAGATTCTGC | 1620 |
| 20 | CAACTGTGGA AACTTCAGTC CCTCAGGCTG GCAGCCATGC CAGTACCTGC CTGGGGGTGG | 1680 |
| | GGGGTGCCCTG GCAGCCATGA AGCAGGCTGA AAGGCAGAGG GGCTCCAGGT CCTGTTTCCA | 1740 |
| 25 | GCTCCCTCA CTGCACATGG TGAAGCTCGC TCCCTCCCTC CCTCCCTTCC CGCTTTTCCC | 1800 |
| | AGAGCTAATA CACAGGTGCT ATTATTCAGA AAAAACTGG TCAGCTCTAG CCAACAGTGA | 1860 |
| | AGGTTTCTTT TCTTCTGCCC TNAACTATTG TGTAGCCTCT TATGCTGAAA TCGGCTTCTG | 1920 |
| 30 | CTGGCTTCTC CGCTTTCAG AGCCCTGAAA CAAAGAGAAA CAGGATCTGT CCTACCCAG | 1980 |
| | CACAGCAAAT GGTGTAGTA ATTGCCAAG CCTCATAAA GCCCTCCGGC TTGAGGAGAG | 2040 |
| 35 | AGTGTATAGT CATGGTTCT GCCTCTGTGC CCTGTCTGGC CGCTTCTCCT CTGCCTTCTT | 2100 |
| | TCCTGGAACT CAGGGTGTGG GGA CTGAGCC TGTAGGGGAC AGCATGCCGT CTGCTGTGG | 2160 |
| | CCACTCCCAA GTGTGCCCTC TTCCCTCTTT ACACATCAGG TGTCTCTGGC ACAGGACTTG | 2220 |
| 40 | GCACTAAGCT CCATGCTGAG ACACCAGGCT ATGTGGGCCC CCACCTTGT TCCAGCCTG | 2280 |
| | CACCTTAGAA GCCGAAGTGC TTTCATCAGA ACCCTAAAAT GGTGTTGAA GCGCCTGGG | 2340 |
| 45 | CCGCAGCCAG CAGTAGTTGG AGAGGCAGGC AGAGGGCAGT GGTTCCTCCA AATAGGAGAC | 2400 |
| | CTGGGGCCTG GCCAGGCAGG GTTTGGGCCT AATGGCTTTG ACTAAATTAC CCCATCCTC | 2460 |
| | CTTGCCCGGA AAAGGGAGAG CTAGAGCCAC TCACTGTCTAT TCTGCTCTGA CCTTGAAGGG | 2520 |
| 50 | GGCGGTGTTG GCCTGGCTTC TGAATGGAC TGAGTCCATC GTGGAAAGGG CTGGGGCAG | 2580 |
| | GAGGAGGTGG GGAGGGGCAC TGCCTGCGGA AGGTAGGATT AGATCATTAG CTCAGTGACC | 2640 |
| 55 | TCCTAGGGTT TCGATGTGCT ATGTTCTCAT CCTACAGTTG GTTTGGTAAT GATCTGCAAG | 2700 |
| | TCCCGGAGAG CAACAGCACA GCTCTGCCTG ACGCTCTCAT TAAAACTAT GCAGCCAAGC | 2760 |
| | TCGGCACTTT GTAGCAGCCG GCCTTGCGAA GCCTCCTCAG CTCGGGGGGC CGGGGACCCA | 2820 |
| 60 | GTGAGCCGNA GAKSTCTGG GCTCCACTTA TGCATATGCA CCAAAAAAAAA AAAAAAAAAA | 2880 |

AAAAGGGGG CGCTCTANA AGGATTCTC NAAGGGGCC AAG

2923

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(2) INFORMATION FOR SEQ ID NO: 27:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 775 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

| | |
|---|-----|
| GAAGTAGTGN ATCCCCGGG CTGCAGGAAT TCGGCACGAG CCCRACCCSC ACCACCACCA | 60 |
| GAATGCAGTT CCAGCTTAGG AAGCCACAAA CAAGCCACCC AGGAGGAACA AAACACCGCC | 120 |
| AGCGTGGATT TTCCCAAATT TCCCTGGAAA GTAAGTCTCG CTCTTGCCAA AGAAAAGTCT | 180 |
| GGCTTGAGAG GTCTCTGGAG CCCAGGATGC CAGCATGTGC CAATGACTGT CACCTTCATC | 240 |
| TCTTCAAAG AAAAGCCATA GCCGAGGACT GTCCCGGAC CCCCGTGAC TCGCTCTAGG | 300 |
| TCATGTGATT CTGTTTCAT TTCTCATCCC ATCCAATTG TCCTTTCTC CTGTCATTTT | 360 |
| CTTCTCTGT GGTCCCTTCA AAGTTGTAT AATTGTACT GAAGTTCAA ATGTGTCCCG | 420 |
| TTCTCCCGAG ACCACTCTAG CCACAGTATA TTGCAATAAA ATTACTTCTT ATATTTCAG | 480 |
| AAATTCCTTT GGTGTAATTT TATTTTTC TCTCAATATA TATAATTGGA CAAACGCTGG | 540 |
| CAAAAAGAAA AAAATGGTAA GCAAAAACC CAAGATAAAG TTTGAGGAC ATCAGGCCTT | 600 |
| TTGAAATACA ATGTCAAATG ACACATTGTA CGKTTTCAA AAATCCGCTA GACATGTCAT | 660 |
| AAGTTTAAAC TGTAATGCCC AGGAAAGGAT ATCTTAAAT ATTCTAACT TGTGTAACAA | 720 |
| AGGAATAATT AACTGTAATA GTTTTCAAT AAATCGAGTT GGGTGTTC ACCGT | 775 |

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(2) INFORMATION FOR SEQ ID NO: 28:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 534 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

| | |
|---|-----|
| GAATTCGGCA CGAGCAAGG TGGAACCTGA GTCTGCTTGT CTGTTTGCC CATGACAGCC | 60 |
| CAGGGGTGGT GGSCTACCC CACCTCCAG CAMCCACAAG AATATAAAT CTGTACAAR | 120 |
| GATGTCGATA TTAATATTGS CATTCCCAAG TGCACCTGCA CCTGTAGTAT CAGGTGGTTT | 180 |

GCAGCCTTGG CTGCATAGCT GCATATGAGA ATCACCTGGG AAGCTTTTAA AAATCCCAGT 240
ATCCCCACCT CTTCCCCAGT TACAGTGGAG TCTTGCGGGT GGTGGGGGAC ATCAATTATT 300
5 TTTGAAAGCT CCMAAGTAAT TCTGGTGTGC AGTGGGGTGA CCAGCTGTCC CAGGGAMCTC 360
CTTTAAAAAA TAATATCCCG GGCACATGAC AGGCCAATTG CCTAATGCA ACCAAGGTTA 420
10 AGAACTACTG GTTTAATGGG AAAATATTTT TTTCNGTGC TTGAATAATA CTGGTTTAT 480
TAAACTCCNG AATCCCATT TTTTCCTTGC CAAATTTTTT AAAGGCNAAA AAAA 534

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(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:
20 (A) LENGTH: 1827 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

NNCNGCAGG GCNCGGTCTT GTCCCGTCAG CGTCCCGCCA GCCAGCTCCT TGCACCCCTC 60
GCGGCCGAGG CGCTCCCTGG TGCTCCCGC GCAGCCATGG CTCAGCACTT CTCCCTGGCC 120
30 GCCTGCGACG TGGTCGGATT CGACCTGGAC CACACTCTGT GTCGCTACAA CCTGCCCGAG 180
AGCGCCCGC TCATTTATAA TAGCTTTGCC CAGTTCCTAG TTAAGGAGAA AGGGTACGAT 240
35 AAGGAATTGC TCAATGTGAC CCCAGAGGAT TGGGATTCTT GTTGCAAAGG TTTGGCATTG 300
GATCTAGAAG ATGGGAACCT CCTTAAACTT GCAAATAATG GCACTGTTCT CAGGGCAAGC 360
CATGGCACCA AGATGATGAC TCCAGAGGTG CTGGCAGAGG CATATGGCAA GAAAGAGTGG 420
40 AAGCACTTCT TGTCGGACAC TGGAAATGGT TGCCGCTCAG GAAAGTATTA CTTTTACGAC 480
AACTACTTTG ACCTGCCAGG AGCTCTTCTG TGTGCCAGGG TGGTGGACTA TTTAACAAAA 540
45 CTGAACAATG GTCAAAAAAC ATTTGATTIT TGGAAGGATA TAGTTGCTGC TATACAACAC 600
AATTATAAAA TGTCAGCTTT TAAGGAAAC TGTGGAATAT ATTTTCAGA AATAAAAAGA 660
GATCCAGGCA GATATTTACA TAGTTGCTCT GAATCTGTGA AAAAATGGCT TCGACAGCTA 720
50 AAGAATGCTG GGAAATTTCT TCTGTTAATT ACCAGTTCTC ACAGTGATTA CTGTAGACTT 780
CTCTGCGAAT ATATCTTGG GAATGATTTT ACAGACCTTT TTGACATTGT GATTACAAAT 840
55 GCATTGAAGC CTGGTTTCTT CTCCCACTTA CCAAGTCAGA GACCTTTCOG GACTCTGAG 900
AATGATGAGG AGCAGGAGGC ACTGCCATCT CTGGATAAAC CTGGCTGGTA CTCCAAGGG 960
AACGCTGTCC ACCTCTATGA ACTTCTGAAG AAAATGACTG GCAAACCTGA ACCCAAGGTT 1020
60

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|----|---|------|
| | GTATTATTTTG GTGACAGCAT GCATTTCAGAT ATTTTCCAG CTCGTCACCTA TAGTAATTGG | 1080 |
| | GAGACAGTCC TCATCCTGGA AGAACTCAGA GGGGATGAAG GCACGAGGAG TCAGAGGCCT | 1140 |
| 5 | GAGGAGTCAG AGCCTCTAGA GAAGAAAGGA AAATATGAGG GACCAAAAGC AAAACCTTTA | 1200 |
| | AATACTTCAT CTAATAAATG GGGCTCTTTT TTTATTGATT CAGTTTGGG ACTGGAAAAT | 1260 |
| 10 | ACAGAAGACT CCTTGGTTTA TACATGGTCT TGTAAAGAGAA TCAGTACTTA CAGCACTATT | 1320 |
| | GCAATTCCAA GTATGAAGC AATCGCAGAA TTACCTCTGG ACTACAAATT TACAAGATTC | 1380 |
| | TCTTCAAGCA ATTCAAAAC AGCTGGCTAC TATCCAAATC CTCCTACTGGT CTTATCAAGT | 1440 |
| 15 | GATGAGACAC TGATATCCAA ATAAGTTGTC TTTACTGAAA AATGAAGTGA AGACCCATAT | 1500 |
| | ATGCAGTTAA AAAAAAGTTA ATTTTCAAAA AATACTGTAA AAGACTTTAA GGAACAAGTT | 1560 |
| 20 | TTATGACCA ATAAGTTGAT ATTTGTCCAT AGGTCTCCTT TCTATAAATC ATCTTGATGT | 1620 |
| | TTAACAATC TTATTATATT AAAATCTCAG TATCCTAAAA CTTAGGAACC TTATTGGATA | 1680 |
| | TTTTCTATTA CAGTAGTTTT GTGGTTGGGA TTCACCCGGG GGGGCCACAC ACTCACACGG | 1740 |
| 25 | CACAGTTCAC TCTTTACACA TATGGCCNCG GTCCCGTGGG GTTCTCNAAG GTGTGGTTCC | 1800 |
| | CTTGGGGCCT NITGGGCTTG GGCCTTT | 1827 |

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(2) INFORMATION FOR SEQ ID NO: 30:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1479 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

| | | |
|----|---|-----|
| | GGCAGAGGG CGGTGGCAT CAGCAGAGGG GCACCAGCCA AAGGGTGTGG CTACCTCACT | 60 |
| | GCTGGTCCCC AGGCCCGGA GGTGGGAGC ACACACAGTG CCTTGGGTAC CCAGNTGGGT | 120 |
| 45 | GTCTCCCCG TCAGAGGAG ACRGCAGCCT GGTCTCTGCC CTTACCTCT GCGGCTTTC | 180 |
| | TCTACATCGC CTTGGTGAAC GTGCTCCCTG ACCTCTTGA AGAAGAGGAC CCGTGGCGCT | 240 |
| 50 | CCCTGCAGCA GCTGCTTCTG CTCTGTGCG GCATCGTGGT AATGGTGCTG TTCTCGCTCT | 300 |
| | TCGTGGATTA ACTTTCCCTG ATGCCGACGC CCCTGCCCCC TGCAGCAATA AGATGCTCGG | 360 |
| | ATTCACTCTG TGACCGCATA TGTGAGAGGC AGAGAGGGCG AGTGGCTGCG AGAGAGAATG | 420 |
| 55 | AGCCTCCCCG CAGACAGGAG GGAGGTGCGT GTGGATGTAT GTGGTGTGCA CATGTGGCCA | 480 |
| | GAGGTGTGTG CCGAGACCG ACACTGTGAT CCCTGTGCTG GGTCCGGGGC CCAGTGTAGC | 540 |
| 60 | GCCTGTCCCC AGCCATGCTG TGGTTACCTC TCCTTGCCGC CCTGTACCT TCACCTCCTG | 600 |

GAGTAAGCAG CGAGGAAGAG CAGCACTGGT CCCAAGCAGA GGCCTTGCCC TGCTGGGACC 660
 CCGGGAGTGA GAGCAGCCCA AGAATCCCAG GGTGCAGGGA ACTCCAGAGC TGCCCACTC 720
 5 CCACTGCCCC CTCAGCACAC ACACAGTCCC CAGGCGGCCT AGGGGCCAAG GCTGGGGCGG 780
 CTTTGGTCCC TTTTCCTGGC CCTTCCTTCC CCACCTCTAA GCCAAAGAAA GGAGAGGCAG 840
 10 GTGCTCCTGT ACCCCAGCCC CACTCAGCAC TGACAGTCCC CAGCTCCTAG TAGTGAGCTG 900
 GGAGGCGCTT CCTAAGACCC TTTCCTCAGG GCTGCCCTGG GAGCTCATTG CTGGCCAACA 960
 CGCCCTGGCA GCACCAGCAG CTCTTGCCAC CTCCAGCTGC CAAACAGCAG CCTGCCGGGC 1020
 15 AGGGAGCAGC CCCAGGCCAG AGAGGCCTCC CGGTCCAGCT CAGGGATGCT CCTGCCAGCA 1080
 CAGGGGCCAG GGAATCCTGG AGCAGGCACA TAGTGAGCCC GGCAGCCCT GCCCAGCTCA 1140
 20 GGCCCCITTC CTTCCTCATT GAGGTGGGG TAGGTGGGG CGGTGAGGGC TCCACGTGT 1200
 CAGCGCTCAG GAATGTGCTC CGGCAGAGTG CTGAAGCCAT AATCCCCAAC CATTTCCCTT 1260
 GGCTGACGCC CAGGTACTCA GCTGGCCAC TCCACAGCCA GGCCTGCCCT GCCCTTACC 1320
 25 GTGGATGTTT TCAGAAGTGG CCATCGAGAG GTCTGGATGG TTTTATAGCA ACTTTGCTGT 1380
 GATTCCGTTT GTATCTGTAA ATATTTGTTC TATAGATAAG ATACAAATAA ATATTATCCA 1440
 30 CATAAAAAAA AAAAAAAAAA AACTTGGGG GGGNCCCG 1479

35 (2) INFORMATION FOR SEQ ID NO: 31:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 987 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

45 GGCACGAGCG CAATCGCGTT TCCGAGAGA CCTGGCTGCT GTGTCCCGG GCTTGGGCTC 60
 CGTAGTGGAC TCCGCGGGCC TTCGGCAGAT GCAGGCCTGG GGTAGTCTCC TTTCTGGACT 120
 GAGAAGAGAA GAATGGAGAA GCCCCTCTTC CCATTAGTGC CTTTGCAITG GTTTGGCTTT 180
 50 GGCTACACAG CACTGGTTGT TTCTGGTGG ATCGTTGGCT ATGTAAAAAC AGGCAGCGTG 240
 CCGTCCCTGG CTGCAAGGCT GCTCTTCGGC AGTCTAGCCG GCCTGGGTGC TTACCAGCTG 300
 55 TATCAGGATC CAAGGAACGT TTGGGGTTTC CTAGCCGCTA CATCTGTTAC TTTTGTGGT 360
 GTTATGGGAA TGAGATCCTA CTAATATGGA AAATTCATGC CTGTAGGTTT AATTGCAGGT 420
 GCCAGTTTGC TGATGGCCGC CAAAGTTGGA GTTCGTATGT TGATGACATC TGATTAGCAG 480
 60

AAGTCATGTT CCAGCTTGA CTCATGAAGG ATTAAAAATC TGCATCTTCC ACTATTTTCA 540
ATGTATTAAG AGAAATAAGT GCAGCATTIT TGCA CTGAC ATTTTACCTA AAAAAAAAAA 600
5 GACACCAAAT TTGGCGGAGG GGTGGAAAAT CAGTTGTTAC CATTATAACC CTACAGAGGT 660
GGTGAGCATG TAACATGAGC TTATTGAGAC CATCATAGAG ATCGATTCTT GTATATTGAT 720
TTTATCTCTT TCTGTATCTA TAGGTAAATC TCAAGGGTAA AATGTTAGGT GTTGACATTG 780
10 AGAACCCCTGA AACCCCATTC CCTGCTCAGA GGAACAGTGT GAAAAAAAAAT CTCTTGAGAG 840
ATTTAGAATA TCTTTTCTTT TGCTCATCTT AGACCACAGA CTGACTTTGA AATTATGTTA 900
15 AGTGAAATAT CAATGAAAAT AAAGTTTACT ATAAATAAWA AAAAAAAAAA AAAAAAAAAA 960
AAAAAAAAA AAAAAAAAAA ANANAAA 987

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(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:
25 (A) LENGTH: 2933 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

TCTACCTCCG AGTAGTATTA GACTGTAAAC ACAGTAATAT AGNCGCCATC ATTCGTGAAG 60
GGGTTTCTTT TGCGGGACAG AGGATCAGAT GTTGAGAGTT TGGACAAACT CATGAAAACC 120
35 AAAATATAC CTGAAGCTCA CCAAGATGCA TTTAAACTG GTTTTGCGGA AGGTTTCTG 180
AAAGCTCAAG CACTCACACA AAAACCAAT GATTCCTTAA GGCGAACCCG TCTGATTCTC 240
40 TTCGTTCTGC TGCTATTCGG CATTTATGGA CTTCTAAAAA ACCCATTTT ATCTGTCCGC 300
TTCCGGACAA CAACAGGCT TGATCTGCA GTAGATCCTG TCCAGATGAA AAATGTCACC 360
TTTGAACATG TTAAAGGGGT GGAGGAAGCT AAACAAGAAT TACAGGAAGT TGTGAATTC 420
45 TTGAAAAATC CACAAAATT TACTATTCTT GGAGGTAAAC TTCCAAAAG AATTCTTTTA 480
GTTGGACCCC CAGGACTGG AAAGACACTT CTTGCCCGAG CTGTGGCGGG AGAAGCTGAT 540
50 GTTCCTTTT ATTATGCTTC TGGATCCGAA TTTGATGAGA TGTTTGTTGG TGTGGGAGCC 600
AGCCGTATCA GAAATCTTT TAGGGAAGCA AAGCGAATG CTCCTTGTGT TATATTAT 660
GATGAATTAG ATTCTGTTGG TGGGAAGAGA ATTGAATCTC CAATGCATCC ATATTCAAG 720
55 CAGACCATAA ATCAACTTCT TGCTGAAATG GATGGTTTAA AACCAATGA AGGAGTTATC 780
ATAATAGGAG CCACAACTT CCCAGAGGCA TTAGATAATG CCTTAATACG TCCTGGTCGT 840
60 TTTGACATGC AAGTTACAGT TCCAAGGCCA GATGTAAAAG GTCGAACAGA AATTTTGAAA 900

| | | |
|----|---|------|
| | TGGTATCTCA ATAAAATAAA GTTTGATCAW TCCGTTGATC CAGAA/TTAT AGCTCGAGGT | 960 |
| 5 | ACTGTTGGCT TTTCCGGAGC AGAGTTGGAG AATCTTGTGA ACCAGGCTGC ATTAAAAGCA | 1020 |
| | GCTGTTGATG GAAAAGAAAT GGTACCATG AAGGAGCTGG GAGTTTCCA AAGACAAAAT | 1080 |
| | TCTAATGGG CCTGAAAGAA GAAGTGTTGA AATTGATAAC AAAACAAAA CCATCACAGC | 1140 |
| 10 | ATATCATGAA TCTGGTCATG CCATTATTGC ATATTACACA AAAGATGCAA TGCCTATCAA | 1200 |
| | CAAAGCTACA ATCATGCCAC GGGGCCAAC ACTTGNACA TGTGTCCCTG TTACCTGAGA | 1260 |
| 15 | ATGACAGATG GAATGAAACT AGAGCCCAGC TGCTTGCACA AATGGATGTT AGTATGGAG | 1320 |
| | GAAGAGTGGC AGAGGAGCTT ATATTGGAA CCGACCATAT TACAACAGGT GCTTCCAGTG | 1380 |
| | ATTTTGATAA TGCCACTAAA ATAGCAAAGS GGATGGTTAC CAAATTGGA ATGAGTGAAA | 1440 |
| 20 | AGCTTGGAGT TATGACCTAC AGTGATACAG GGAACTAAG TCCAGAAACC CAATCTGCCA | 1500 |
| | TGGAACAAGA AATAAGAATC CTTCTAAGG ACTCATATGA ACGAGCAAAA CATATCTTGA | 1560 |
| 25 | AAACTCATGC AAAGGAGCAT AAGAATCTCG CAGAAGCTTT ATTGACCTAT GAGACTTTGG | 1620 |
| | ATGCCAAAGA GATTCAAATT GTTCTTGAGG GGAAAAAGTT GGAAGTGAGA TGATAACTCT | 1680 |
| | CTTGATATGG ATGCTTGCTG GTTTTATTGC AAGAATAYAA GTAGCATTGC AGTAGTCTAC | 1740 |
| 30 | TTTTACAACG CTTTCCCCTC ATTCTTGATG TGGTGTAATT GAAGGCTGTG AAATGCTTTG | 1800 |
| | TCAATCAITT GTCACATTTA TCCAGTTTGG GTTATTCTCA TTATGACACC TATTGCAAAT | 1860 |
| 35 | TAGCATCCCA TGGCAAATAT ATTTTGAAAA AATAAAGAAC TATCAGGATT GAAAACAGCT | 1920 |
| | CTTTTGAGGA ATGTCAATTA GTTATTAAGT TGAAAGTAAT TAATGATTTT ATGTTTGGTT | 1980 |
| | ACTCTACTAG ATTTGATAAA AATTGTGCCT TTAGCCTTCT ATATACATCA GTGGAACTT | 2040 |
| 40 | AAGATGCAGT AATTATGTTT CAGATTGACC ATGAATAAAA TATTTTAA TCTAAATGTA | 2100 |
| | GAGAAGTTGG GATTAAAAGC AGTCTCGGAA ACACAGAGCC AGGGAATATA GCCTTTTGGC | 2160 |
| 45 | ATGGTGCCAT GGCTCACATC TGTAATCCCA GCACTTTTGG AGGCTGAGGC GGGTGGATTG | 2220 |
| | CTTGAGGCCA GGAGTTCGAG ACCAGCCTGG CCAACGTGGT GAAACGCTGT YTCTACTAAA | 2280 |
| | ATACAAAAAA ATAGGGCTGG GCGCGGTTGC TCACGCTGT AATCCCAGCA CTTTTCAGAG | 2340 |
| 50 | GCCAAGGCGG GCAAATCACC TGAGGTCAAG AGTTTGAGAC CAGCCTGGCC AACATGGTGA | 2400 |
| | AACCCCATCT CTAATAAACA TGCAAAAATT ACCTGGGCAT GGTGGCAGGT GCTTATAATC | 2460 |
| 55 | CCAGCTACTC TGGGGGCCAA GGCAGGAGAA TTGCTTGAGC CTGGGAGATG GAGGTTCAG | 2520 |
| | TGAGCTGAGA TCATGCCACT GCACTCCAGC CTGGGCAACA GAGCAAGACT CTGCCTCAAA | 2580 |
| | AAAAAATTAA AATAAATTTA AATACAAAA AAAATAGCCA GGTGTGGGT GCATGCCTGG | 2640 |
| 60 | AATCCAGCT ACTTGAGAGG CTGAGGCAG AGAATGCTT GAACCCAGGA GGTGGAGGTT | 2700 |

GCAGTGAGCC AAGATCACAG GAGCCACTGC ACTCCAGCCT GGGTGACAGA GTGAGACTTT 2760
GTCTCAAAAM AAAATTAAAT AAATTATTAT AACCTTTCAG AAATGCTGTG TGCATTTC 2820
5 TGTCTTTTTT TTTAGCATTA CTGTCACTCT CCCTAATGAA ATGTACTTCA GAGAAGCAGT 2880
ATTTTGTAA ATAAATACAT AACCTCAAAA AAAAAAAAAA AAAAAAACT CGA 2933
10

(2) INFORMATION FOR SEQ ID NO: 33:

15 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1366 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear
20
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

GGGAATACCT ATTCTCCTTT ACCGTGTGTC TTTTCCCCCT GGAATTGAGC CAGCAAGTTC 60
25 TTGGCATGGC AGGTGTTTCT GAAATATCAG TGTGTTTTTY TTTGCTTTCT TTGTTTTCCT 120
TGTMTTGCTC TTTCTATTTT CCTAAGCAGG CAACTCCAAA AAGAGATTTG TTTGTGCAGG 180
AGTCAGGAAA AGGGAAGAGG AATACTGAAA GCTGGGAGTA GGGCAGGACA GAAGAGGGGG 240
30 AGGAGTCTAT TTTCAATTGT TAAGTKTTGA ACTTCCACCA ATGCCAAAGT CACGGACATG 300
TGTGCACTTG GATGTCGAG TTAGAGCAGC CCCAAGGGCC TGTAACTGA ATAGCAGGCA 360
35 CTCACCCAGC TGATAACTCA AGTTCCAAAT GGACCACAGC TGAGTTGTAG GGGATGTGTG 420
TGTGTGTGTA CGCGTGGGTT TGAGATTTCCT GGAACAGATT TCCTCTGAGA TCTCAACAGG 480
CTTTTTCATT ATCATTTGGG AGCTATGGTT TCTCTTATTT CACAAGGCCC ATTCTTTCCT 540
40 TTTGAGATGT GCAAGGAGAT GACTCCATCC ATGACTTGGC TTTACACTCT CCTCCTTGG 600
CTTTTATCA TCAGTGCAGR AGARATTCCT GCTCGTCTTT CAAACAATCT CATTCGAGCT 660
45 TTATAAAGAT TATTGGARTT TAAATAATAT TCATATCTAT GGCCTAGAAC AATGTTCTCT 720
AAGTATGCGT CAGAATCATG AGTGGTAGAG GGAGGATTAT AATGTAGTTT CCTACATTTC 780
TACCTCCAC CACCTGGAG TCTGCATTTT AACGTACTTC TGTVTGAGGA TCAGAYTTTG 840
50 GGAAGCGTTG GGCTTGAGAT GTTTTCTKGA CATTGATTTA TGTGAGACC AGACCAAGAA 900
GCAGATGGAT GGACATGATC AGTTCATAAA CATGTTCTTT TCTTAGGGTC AAATTGGAGG 960
55 AGGCTCTAGA GAAGCACTGT CCAATAGAAA TATAATGCCA ACAATATATG TWATTTTAAG 1020
TCCTCTATTG GTGCATTTAA AAAGTAAAAG AAGGCTGAGT GGCTGGGCAT GGCTCCTCGT 1080
GCCTGTAATC CCAGCACTTT GGGAGGCCGG GGTGGGCAGA TCACCTGAGG TCAGGAGTTC 1140
60

GAGACCAGCC TGCCCAACAT GGTGAAACCC CATATNTACT AAAAATACAA AAAATTAACC 1200
GGGCATAGTG GCAGGTGCCT GTAATCCCAG CTACTCGGGA GGCTGAGGCA GGAGAATCGC 1260
5 TTGAACCTGG GAGGCAGAGA CTGCAGTGAG CTGAGATCGT GCCACTACAC TCCAGCCTGG 1320
GTGATGAGCG AAATCCGTC TCAAAAAAAA AAAAAAAAAA ACTCGA 1366

10

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:
15 (A) LENGTH: 667 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

ATTTTCGGCA CAGGCCGGAA GCTACCTATC TGGTAGGGAG CTCCCCCAGC ACCGAAGACT 60
GCGATGACTT CTGCRCTGAC CCAGGGGCTG GAGCGAATCC CAGACCAGCT CGGCTACCTG 120
25 GTACTGAGTG AAGGTGCAGT GCTGGCGTCA TCTGGGGACC TGGAGAATGA TGAGCAGGCA 180
GCCAGTGCCA TCTCTGAGCT GGTGAGCACA GCCTGCGGTT TCGGCTGCA CCGCGGCATG 240
30 AATGTGCCCT TCAAGCGCCT GTCTGTGGTC TTGGGAGAAC ACACACTGCT GGTGACGGT 300
TCAGGACAGA GGGTGTGTTGT GGTGAAGAGG CAGAACCGAG GTCGGGAGCC CATTGATGTC 360
TGAGCCTGCC GGAGGGCGAG GGTGCGAGAA GCGGATTGGG TCCTGGGCCT CTGTGATGAG 420
35 GCAGGCACAN CTGTGGTCTT TGGCTTGCTG CTAGAACTAG GGCCTTCTGC TCGCCACCT 480
CCCACCCCTA CCTGGACGGG CCCAGGCTTG GGGACTCTGA GCTGTGTTAA GGAGAACAAG 540
40 GGCAAGGAGA CCTCCCTTTG TGCTCCCTCA CTCCCTAATA AACATGAGTC TGATGTTCTC 600
CARMMMAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 660
AAAAANN 667

45

(2) INFORMATION FOR SEQ ID NO: 35:

50 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1710 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
55 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

60 GGCACGAGCC AGAGCAGGCT GCTAGGCCTG GGGCCACCAC TGCCCTGGG TGCTACACCC 60

| | | | | | | | |
|----|-------------|-------------|------------|------------|------------|------------|------|
| | AGTGTGCTGG | GTCACCTGGGA | ACTTCCTGAA | GTGGTGTAC | CTGAACTGGG | CCCCAAGGA | 120 |
| | TGGGGTGCGG | GCAGTACCGC | AGGAAGAGGA | GCAGCCCCTG | TGAAGATTGA | GAGCTGCCAG | 180 |
| 5 | AGGCTCTGTG | ATTGGCTGCG | GCACGATGAC | CCGCGCACGG | ATTGGCTGCT | TCGGGCCGGG | 240 |
| | GGGCCGGGCC | CGGGGACAG | AATCCGCCCC | CGAACCTTCA | AAGAGGGTAC | CCCCCGGCAG | 300 |
| 10 | GAGNTGGCAG | ACCTTAGGAG | GTGCGACAGA | CCCGCGGGGC | AAACGGACTG | GGGCCAAGAG | 360 |
| | CCGGGAGCGC | GGGCGCAAAG | GCACCAGGGC | CCGCCAGGG | CGCCGCGCAG | CACGGCCTTG | 420 |
| | GGGGTTCTGC | GGGCCTTCGG | GTGCGCGTCT | CGCCTCTAGC | CATGGGGTCC | GCAGCGTTGG | 480 |
| 15 | AGATCCTGGG | CCTGGTGTG | TGCCTGGTGG | GCTGGGGGGG | TCTGATCCTG | GCGTGGGGGC | 540 |
| | TGCCCCATGTG | GCAGGTGACC | GCCTTCCTGG | ACCACAACAT | CGTGACGGCG | CAGACCACCT | 600 |
| 20 | GGAAGGGGCT | GTGGATGTG | TGCGTGGTGC | AGAGCACNGG | GCACATGCAG | TGCAAAGTGT | 660 |
| | ACGACTCGGT | GCTGGCTCTG | AGCACCGAGG | TGCAGGCGGC | GCGGGCGCTC | ACCGTGAGCG | 720 |
| | CCGTGCTGCT | GGCGTTCGTT | GCGCTCTTCG | TGACCCTGGC | GGGCGCGCAG | TGCACCACCT | 780 |
| 25 | GCGTGGCCCC | GGGCCCCGCC | AAGGCGCGTG | TGGCCCTCAC | GGGAGGCGTG | CTCTACCTGT | 840 |
| | TTTGCGGGCT | GCTGGCGCTC | GTGCCACTCT | GCTGGTTGCG | CAACATTGTC | GTCCGCGAGT | 900 |
| 30 | TTTACGACCC | GTCTGTGCCC | GTGTGCGAGA | AGTACGAGCT | GGGCGCANGC | TGTACATCGG | 960 |
| | CTGGGCGGCC | ACCGCGCTGC | TCATGGTAGG | CGGCTGCCTC | TTGTGCTGCG | GCGCCTGGGT | 1020 |
| | CTGCACCGGC | CGTCCCGACC | TCAGCTTCCC | CGTGAAGTAC | TCAGCGCCGC | GGCGGCCAC | 1080 |
| 35 | GGCCACCGGC | GACTACGACA | AGAAGAACTA | CGTCTGAGGG | CGCTGGGCAC | GGCGGGCCCC | 1140 |
| | CTCCTGCCAG | CCACGCCCTG | GAGGCGTTGG | ATAAGCCTGG | GGAKCCCCGC | ATGGACCGCG | 1200 |
| 40 | GCTTCCGCGG | GGTAGCGCGG | CGCGCAGGCT | CCTCGGAACG | TCCGGCTCTG | CGCCCCGACG | 1260 |
| | CGGCTCCTGG | ATCCGCTCCT | GCCTGCGCCC | GCAGCTGACC | TTCTCCTGCC | ACTAGCCCGG | 1320 |
| | CCCTGCCCTT | AACAGACGGA | ATGAAGTTTC | CTTTCTGTG | CGCGGCGCTG | TTTCCATAGG | 1380 |
| 45 | CAGAGCGGGT | GTCAGACTGA | GGATTTCGCT | TCCCCCTCAA | GACGCTGGGG | GTCTTGGCTG | 1440 |
| | CTGCCTTACT | TCCCAGAGGC | TCCTGCTGAC | TTCCGAGGGG | CGATGCAGA | GCCCAGGGCC | 1500 |
| 50 | CCCACCGGAA | GATGTGTACA | GCTGGTCTTT | ACTCCATCGG | CAGGCCCGAG | CCCAGGGACC | 1560 |
| | AGTGACTTGG | CCTGGACCTC | COGGTCTCAC | TCCAGCATCT | CCCCAGGCAA | GGCTTGTGGG | 1620 |
| | CACCGAGCT | TGAGAGAGGG | CGGGAGTGGG | AAGGCTAAGA | ATCTGCTTAG | TAAATGGTTT | 1680 |
| 55 | GAACTCTCAA | AAAAAAAAAA | AAAAAAAAAA | | | | 1710 |

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1096 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

10 GGCCAGTGGG CAGGGTCACA GGGCAAGTTC CCGGGGGCCG CTGGGTGCGG CGACTTCCGT 60
GCTCCCGGCG AGCGGGCGGA GAGCGGGGGC CGCACTGGGG AGTGTGGGCT GGGCCGCAGA 120
TGTCATGTGG CCGTGTCTTT GGACCGTGGT TCGTACCTAT GCTCCTTATG TCACATTCCC 180
15 TGTGCGCTTC GTGGTCGGGG CTGTGGGTTA CCACCTGGAA TGGTTCATCA GGGGAAAGGA 240
CCCCCAGCCC GTGGAGGAGG AAAAGAGCAT CTCAGAGCGC CGGGAGGATC GCAAGCTGGA 300
20 TGAGCTTCTA GGCAAGGACC ACACGCAGGT GGTGAGCCTT AAGGACAAGC TAGAATTGTC 360
CCCGAAAGCT GTGCTGAACA GAAACCGCCC AGAGAAGAAT TAATGGAGGA CACAGGGCCC 420
TATGGTCTTA CTGTGGGTGG TGACTTGTCC TGCTACCATG TTGACAGAGC CCCAGAAGCC 480
25 ACATCTAATT GCGTTTGTGG CTTATTCTGG CCCTTCCAC ACCACACAGC CACACAAATA 540
CTGGCTGCTC CTTGATGGCC AGGCAGACCC AGCAGCAGCC GAGGGGCCAG TGAAGAGGAA 600
30 GGCCGCATCT GTTGTGTGGT GGCCACAAGC ACTCAGGCAT CTGAGTTTAC TGGTGCACTG 660
CTGGGAGGAG AGTTATGAGA TGAACATGG CTGTCAATCT CTGTGGGCAG GCGGTTTGGC 720
CTCTAGTGGG AATGGCTGGG ATTTGGGCGT TGCCTTTAGG AGGGATACCT GCATGTCTAG 780
35 TTCCAGTCTG CACTGGAAG AATTCAAATA TGCACCTGGC TCCCTTCACT ATTTTGCCT 840
ATCCTTTGTG CTCATTCTTA CTGAAATCTG TCTTGTGAGC TCAGGAATGG GATTCCCCCA 900
40 GGAAGGAAAG CACTTTTCTG TTCTGGGAAG CCCAGACTGT TCACTTTGGG GCAGGGACGA 960
ACATGTGCCT CGTGAATTG CTTGAAAACA GTCACCATCT TCTACCCCCA TCACTGTATA 1020
GTGAAAAACC TGATTAAAGT GGTATCTGAG AACCAWAAAA AAAAAAAAAA AAAAAAAAAA 1080
45 AAAAANGGGG GGNCCC 1096

50

(2) INFORMATION FOR SEQ ID NO: 37:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2279 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

60

| | | |
|----|--|------|
| | GGTGGGCAAG GGGCTCAGCT CGCAGCGCAT GCCCGCGCAC AGGTTGCTGC TGGCCGTGGG | 60 |
| | CAGCGCCGTC TTAAATGCCA TGTTC AACCG GGGMATGGCC ACAACATCCA CGGAGATTGA | 120 |
| 5 | GCTGCCCCGAC GTRGAACCCG CCGCCTTCCT CGCACTGCTC AAGTTTCTCT ACTCGGACGA | 180 |
| | GGTGAGATT GCGCCGGAGA CGTGATGAC CACGSTATAC ACCGCCAAGA AGTACGCGGT | 240 |
| 10 | GCCAGCGCTC GAGGCCCAT TCGTGAGATT CCTGAAGAAG AACCTGCGAG CCGACAACGC | 300 |
| | CTTCATGCTG CTCACGCAGG CGGACTCTT CGATGAACCG CAGCTGGCCA GCCTGTGCCT | 360 |
| | GGAGAACATC GACAAAAACA CTGCAGACGC CATCACCGCG GAGGGCTTCA CCGACATTGA | 420 |
| 15 | CCTGGACACG CTGGTGGCTG TCCTGGAGCG CGACACACTG GGCATCCGTG AGGTGCGGCT | 480 |
| | GTTCAATGCC GTTGTCCGCT GGTCCGAGGC CGAGTGTGAG CGGCAGCAGC TGCAGGTGAC | 540 |
| 20 | GCCAGAGAAC AGGCGGAAGG TTCTGGGCAA GGCCCTGGGC CTCATTGCT TCCCGCTCAT | 600 |
| | GACCATCGAG GAGTTCGCTG CAGGTCCCGC ACAGTCGGGC ATCCTGGTGG ACCGCGAGGT | 660 |
| | GGTCAGCCTC TTCTGCACTT CACCGTCAAC CCAAGCCAC GAGTGGAGTT CATGTACCGG | 720 |
| 25 | CCCCGCTGCT GCCTGCGTGG GAAGGAGTGC AGCATCAACC GCTTCCAGCA GGTGGAGAGT | 780 |
| | CGCTGGGGCT ACAGSGGGAC CAGTGACCGC ATCAGGTTCT CAGTCAACAA CGGCATCTTC | 840 |
| 30 | GTGGTGGGAT TTGGGCTGTA TGGATCCATC CACGGGCCCA CCGACTACCA AGTGAACATC | 900 |
| | CAGATTATTC ACACCGATAG CAACACCGTC TTGGGCCAGA ACGACACGGG CTTCAGCTGC | 960 |
| | GACGGCTCAG CCAGCACCTT CCGGTCATG TTCAAGGAGC CGGTGGAGGT GCTGCCAAC | 1020 |
| 35 | GTCAACTACA CGGCCTGTGC CACGCTCAAG GGCCAGACT CCCACTACGG CACCAAAGGC | 1080 |
| | CTGCGCAAGG TGACACACGA GTCGCCACC ACGGGCGCCA AGACCTGCTT CACCTTTTGC | 1140 |
| 40 | TACGCGCCG GGAACAACAA TGSCATCC GTGGAGGACG GCCAGATCCC CGAGGTATC | 1200 |
| | TTCTACACCT AGGCTGCCG ACACCGACAC CGCCTCCCT CCGTGGGAT AGCCGAGCC | 1260 |
| | CCAGGCCATC ATCTGTGCT GGGGYCCCC CACCACCGG TGCCAGGCC AGTGTCCCC | 1320 |
| 45 | AGGCCGTCTG TCCACTCCAT GCCACCTTTC TCAGCATCAG GACGGGGTTG CCCTGTGTTT | 1380 |
| | ACCACGAGTK TGGCTGCTGG ATCAGGGCAG CCGGGGAGGT GGCCAGGCCA GTGGCCAGGC | 1440 |
| 50 | CCTGTGGAGA CAATCCCTCA GGAAGTGGG CAGGGCTGTG CCGGCCTGGG CCAGGGCCCA | 1500 |
| | CGGACCCGCA GCTCAGGGCG CCGGCCACG TCGTCTGCCG GCGGTGCGCC GCGGGCGTCC | 1560 |
| | CTCGCGTCTC TTCACTGCAC ATTGCAATGC ATTGCGATT CCCATTCTTC TGCTAGGAGC | 1620 |
| 55 | CAGCCTGGGT GCGCTGCTC CCAGAGCGT GGGTCCCAGA CCTTGCGTTC CTTTGTGTTT | 1680 |
| | TGTCCGTTTA TCAGGACACG GGGCCACCT GTCACGTGCC CGAGGCCACC CAAGCCCAGC | 1740 |
| 60 | CTGCGGGGCG TTCCACTGC CTGGATGCCG GCTTGAGTTC TGCGCACGCA GGATTCAATG | 1800 |

TGGGGACGGC CCCTGCCGA TAGGCCTAGC CCTGGCCCAG GTGGTGAGCG GTTTGCAGTG 1860
 TCCGTTCTCA TCCACCTGAT GGGCCCAGAT AAAGGCCCCC GCTGTCCAGC CTCCCTGGAC 1920
 5 GGGCCTCGCG GTCCCTGCAG CCCAAGATGG GACTCAGACC CTGTGCCCCA GAGCTCCCT 1980
 GCGGCAGAAT GGGGCCCCAG CCGGCCCCGA CCGGGTCCAG GAGCACTGCT CGCCTGTACA 2040
 TACTGTGTCC CTAGCCCACC TGGTGCCGTG GGAGCCACCC CCAGGTGCTG GGGCACAGCC 2100
 10 CCTCCCCACT CCGGCCACGC CCCACCCAC CCCGCGTGT TCTGCCCTGT GACTCCTGGA 2160
 ACCTGCGTCC TCCCAAAGC CATGGGAGGG GTGTCTCTCT CAGACCATGC CCCCAGATGA 2220
 15 TTTTITTAAA TAAAGAAACA AATGCACCTG CAAAACAAAA AAAAAAAAAA AAAACTCGA 2279

20 (2) INFORMATION FOR SEQ ID NO: 38:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 745 base pairs
 (B) TYPE: nucleic acid
 25 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

30 GTACAGGACT GAGAAGCAGA TAACAAGAGT GACGCTCACA GGGCTGGGCT GACGCTAACA 60
 GGAGGCAGTG TGTGGCTCGA AGATTCTTGA ACCCACAGCA GCAGCTGCGG CCACCCCATC 120
 CTGCCCACAG CTCCAGCCCT GAGACGACGA GGAGGAGAGT CGACTTTGCC TCTTGCCCAA 180
 35 GGGACCATGC CCAGGTGCCG GTGGCTCTCC CTGATCCTCC TCACCATTCCT CCTGGCCCTG 240
 GTGGCCAGGA AAGACCCAAA AAAGAATGAG ACGGGGGTGC TGAGGAAATT AAAACCCGTC 300
 40 AATGCCTTCA ANTGCCAAGC TGGAAGCAGT GTYYGTGGTT TTGCCATGCA AGAATACAAC 360
 AAAGAGAGCG AGGACAAGTA TGTCTTCCTG GTGGTCAAGA CACTGCAAGC CCAGCTTCAG 420
 GTCACAAATC TTCTGGAATA CCTTATTGAT GTAGAAATG CCCGCAGCGA TTGCAGAAAG 480
 45 CCTTTAAGCA CTAATGAAAT CGCGCCATTC AAGARAATC CAAGCTGAAA AGGAAATTAA 540
 GCTGCAGCTT TTTGGTAGGA GCACCTCCCT GGAATGGTGA ATTCACTGTG ATGGAGAAAA 600
 50 AGTGTGAAGA TGCTTAATGG TGTMTGAGG CATCCCTCCA ACCTCTGTGA CTACTTTATC 660
 CATGAAAATG AAGCAATGGT CAGGTGGGAG GCTCTTCCA ATGTGCTTTC TTCAAAAAAA 720
 AAAAAAAAAA AAAAAAAAAA CTCGA 745
 55

60 (2) INFORMATION FOR SEQ ID NO: 39:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1718 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

| | | |
|----|---|------|
| 10 | CCCCATAGGC AGGAGGCCCC CGGGCAGCAC ATCCTGTCTG CTTGTGTCTG CTGCAGAGTT | 60 |
| | CTGTCCCTGC ATTGGTGCCG CTCAGGCCAG GCTGCACTGC TGGGACCTGG GCCATGTCTC | 120 |
| | CCCACCCAC CGCCCTCCTG GGCCTAGTGC TCTGCCTGGC CCAGACCATC CACACGCAGG | 180 |
| 15 | AGGAAGATCT GCCCAGACCC TCCATCTCGG CTGAGCCAGG CACCGTGATC CCCCTGGGGA | 240 |
| | GCCATGTGAC TTTCGTGTGC CGGGGCCCGG TTGGGGTTCA AACATTCCGC CTGGAGAGGG | 300 |
| | AGAGTAGATC CACATACAAT GATACTGAAG ATGTGTCTCA AGCTAGTCCA TCTGAGTCAG | 360 |
| 20 | AGGCCAGATT CCGCATTGAC TCAGTAAGTG AAGGAAATGC CGGGCCTTAT CGCTGCATCT | 420 |
| | ATTATAAGCC CCCTAAATGG TCTGAGCAGA GTGACTACTG GAGCTGCTGG TGAAAGAAAC | 480 |
| 25 | CTCTGGAGGC CCGGACTCCC CGGACACAGA GCGCGCTCC TCAGCTGGAC CCACGCAGAG | 540 |
| | GCCGTCCGAC AACAGTCACA ATGAGCATGC ACCTGCTTCC CAAGGCCTGA AAGCTGAGCA | 600 |
| | TCTGTATATT CTCATCGGGG TCTCAGTGGT CTTCTCTTTC TGTCTCCTCC TCCTGGTCCT | 660 |
| 30 | CTTCTGCCTC CATGCCAGA ATCAGATAAA GCAGGGGCCC CCCAGAAGCA AGGACGAGGA | 720 |
| | GCAGAAGCCA CAGCAGAGGC CTGACCTGGC TGTGTATGTT CTAGAGAGGA CAGCAGACAA | 780 |
| 35 | GGCCACAGTC AATGGACTTC CTGAGAAGGA CAGAGAGACG GACACCTCGG CCCTGGCTGC | 840 |
| | AGGGAGTTCC CAGGAGGTGA CGTATGCTCA GCTGGACCAC TGGGCCCTCA CACAGAGGAC | 900 |
| | AGCCCGGGCT GTGTCCCCAC AGTCCACAAA GCCCATGGCC GAGTCCATCA CGTATGCAGC | 960 |
| 40 | CGTTGCCAGA CACTGACCCC ATACCCACCT GGCCTCTGCA CCTGAGGGTA GAAAGTCACT | 1020 |
| | CTAGGAAAAG CCTGAAGCAG CCATTGGAAG GGCTTCTGT TGGATTCTCTC TTCATCTAGA | 1080 |
| 45 | AAGCCAGCCA GGCAGCTGTC CTGGAGACAA GAGCTGGAGA CTGGAGGTTT CTAACCAGCA | 1140 |
| | TCCAGAAGGT TCGTTAGCCA GGTGGTCCCT TCTACAATCG AGCAGCTCCT TGGACAGACT | 1200 |
| | GTTTCTCAGT TATTTCCAGA GACCCAGCTA CAGTTCCCTG GCTGTTTCTA GAGACCCAGC | 1260 |
| 50 | TTTATTACCC TGACTGTTTC CAGAGACCCA GCTAAAGTCA CCTGCCTGTT CTAAGGCC | 1320 |
| | AGCTACAGCC AATCAGCCGA TTTCTGAGC AGTGATGCCA CCTCCAAGCT TGTCTAGGT | 1380 |
| 55 | GTCTGTGTG AACCTCCAGT GACCCAGAG ACTTTGCTGT AATTATCTGC CTTGCTGACC | 1440 |
| | CTAAAGACCT TCCTAGAAGT CAAGAGCTAG CCTTGAGACT GTGCTATACA CACACAGCTG | 1500 |
| 60 | AGAGCCAAGC CCAGTTCTCT GGTTGTGCT TTACTCCACG CATCAATAAA TAATTTTGAA | 1560 |

GGCTCACAT CTGGCAGCCC CAGGCCTGGT CCTGGGTGCA TAGGTCTCTC GGACCCACTC 1620
 TCTGCCTTCA CAGTTGTTCA AAGCTGAGTG AGGGAACAG GACCTACGAA AAAAAAAAAA 1680
 5 AAAAAAATCG AGGGGGGGCC CGTACCCAAT CGCCTGTA 1718

10 (2) INFORMATION FOR SEQ ID NO: 40:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1966 base pairs
 (B) TYPE: nucleic acid
 15 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

20 GTCCGCGCTG CAGGTCGACA CTAGTGGATC CAAAGAATTC GGCACGAGCT GGGGAGCGGG 60
 ACTSGAGAAT ACTGCCAGT TACTCTAGCG CGCCAGGCCG AACCGCAGCT TCTTGGCTTA 120
 GGTACTTCTA CTCACAGCG CCGATTCCGA GGCCAACTCC AGCAATGGCT TTTGCAAATC 180
 25 TGCGGAAAGT GCTCATCAGT GACAGCCTGG ACCCTTGCTG CCGGAAGATC TTGCAAGATG 240
 GAGGGCTGCA GGTGGTGGAA AAGCAGAAC TTAGCAAAGA GGAGCTGATA GCGGACTGCA 300
 30 GGACTGTGAA GGCCTTATTG TTCGCTCTGC CACCAAGGTG ACCGCTGATG TCATCAACCC 360
 AGCTGAGAAA CTCAGGTGG TGGCAGGGC TGGCACAGGT GTGGACAATG TGGATCTGGA 420
 GGCCGCAACA AGGAAGGGCA TCTTGGTTAT GAACACCCCC AATGGGAACA GCCTCAGTGC 480
 35 CGCAGAACTC ACTTGTGGAA TGATCATGTG CCTGGCCAGG CAGATTCCCC AGGCGACGGC 540
 TTCGATGAAG GACGGCAAAT GGGAGCGGAA GAAGTTCATG GGAACAGAGC TGAATGGAAA 600
 40 GACCTGGGA ATTCTTGGCC TGGCAGGAT TGGGAGAGAG GTAGCTACCC GGATGCAGTC 660
 CTTTGGGATG AAGACTATAG GGTATGACCC CATCATTTCC CCAGAGGTCT CGGCCTCCTT 720
 TGGTGTTCAG CAGCTGCCCC TGGAGGAGAT CTGGCCTCTC TGTGATTTCA TCACTGTGCA 780
 45 CACTCCTCTC CTGCCCTCCA CGACAGGCTT GCTGAATGAC AACACCTTTG CCCAGTGCAA 840
 GAAGGGGGTG CGTGTGGTGA ACTGTGCCCC TGGAGGGATC GTGGACGAAG GCGCCCTGCT 900
 50 CCGGGCCCTG CAGTCTGGCC AGTGTGCCG GGCTGCACTG GACGTGTTTA CGGAAGAGCC 960
 GCCACGGGAC CGGCCTTGG TGGACCATGA GAATGTCATC AGCTGTCCCC ACCTGGGTGC 1020
 CAGCACCAAG GAGGCTCAGA GCCGCTGTGG GGAGGAAATT GCTGTTTCA TCGTGGACAT 1080
 55 GGTGAAGGG AAATCTCTCA CGGGGTGTG GAATGCCAG GCCCTTACCA GTGCCTTCTC 1140
 TCCACACACC AAGCCTTGA TTGGTCTGGC AGAAGCTCTG GGGACACTGA TCGGAGCCTG 1200
 60 GGCTGGGTCC CCCAAAGGA CCATCCAGT GATAACACAG GGAACATCCC TGAAGAATGC 1260

TGGGAAGTGC CTAAGCCCCG CAGTCATTGT CGGCCTCCTG AAAGAGGCTT CCAAGCAGGC 1320
 5 GGATGTGAAC TTGGTGAACG CTAAGCTGCT GGTGAAAGAG GCTGGCCTCA ATGTCAACCAC 1380
 CTCCCACAGC CCTGCTGCAC CAGGGGAGCA AGGCTTCGGG GAATGCCTCC TGGCCGTGGC 1440
 CCTGGCAGGC GCCCCTTACC AGGCTGTGGG CTTGGTCCAA GGCACCTACRC CTGTACTGCA 1500
 10 GGGGCTCAAT GGAGCTGTCT TCAGGCCAGA AGTGCCTCTC CGCAGGGACC TGGCCCTGCT 1560
 CCTATTCGGG ACTCAGACCT CTGACCTGTC AATGCTGCCT ACCATGATTG GCCTCCTGGC 1620
 AGAGGCAGGC GTGCGGCTGC TGTCTACCA GACTTCACTG GTGTCAGATG GGGAGACCTG 1680
 15 GCACGTCATG GGCATCTCCT CCTGCTGCC CAGCCTGGAA GCGTGAAGC AGCATGTGAC 1740
 TGAAGCCTTC CAGTTCCACT TCTAACCTTG GAGCTCACTG GTCCCTGCTT CTGGGGCTTT 1800
 20 TCTGAAGAAA CCCACCCACT GTGATCAATA GGGAGAGAAA ATCCACATTC TTGGGCTGAA 1860
 CGCGGGCCTC TGACACTGCT TACACTGCAC TCTGACCCTG TAGTACAGCA ATAACCGTCT 1920
 AATAAGAGC CTACCCCAA AAAAAAAAAA AAAAAAAAAA ACTCGA 1966
 25

(2) INFORMATION FOR SEQ ID NO: 41:

30

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 972 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

40 GGCACGAGCC AAGTGGTCCC CCAGACAAGG CTCAGGATGT CCACATCCAC TGCATCCTGG 60
 ACCCTGTGCA GGTGAAGATG TCCCGACCCA CGCATACTCC TCTTTCGCCT GCCACCATTT 120
 CTCCAACCAT CACAGTAGCA GTCTTCTTCG CTGTGTTCGT CGCCGCCGCC GCCGCCACCG 180
 45 CCGTGTGTCG CGTCGCTGCT GCAACCACCA GCAGCGGSCG CAGAACTASA GACAAATCCC 240
 CCATAGCCAC TCAGTCTTCC GTAACCCACA TCGCAGCCAA AAGATGTCAC AACTACACCG 300
 AGTGCCTTTC TTTGATCAGG ARGACCCGGA TTCCTACCTG GARGARGARG ACAACCTGCC 360
 50 CTCCCGTAT CCAAGTACC CACGTGCGGG CTGGGGCGGG TTTTATCAGA GAGCGGGCCT 420
 GCCTCCAATG TGGGGCTGTG GGGCCACCAG GGTGTATCCT GGCCAGTCTG CCACCACCTT 480
 55 CTCTCTACCT GTCACCTGAG CTGCGCTGCA TGCCCAAGCG TGTAGAGGCC AGGTCTGAGC 540
 TGAGGCTCTG CCGCCTGGC GTCMTCTGAC TACCTCTGCC TCCCTCACGG TGTGGACGA 600
 60 GGCTCCCAT CAACGGACCC CAGCTCCAAG CTCAGTCTG GTCCCCCATT CCTCCAGCC 660

CTGGCCCAAA GTCCAGGCTG CGGACCCTGC CCCTCCCCCG ACCATGTTTG TCCCACTCAG 720
CCGGAATCCA GGGGGCAATG CC ACTACCA GGTGTACGAC AGCCTGGAGC TGAAGCGGCA 780
5 GGTGCAGAAG AGCAGAGCCA GGTCCAGCTC ACTGCCACCG GCTTCCACCT CCACCTTGAG 840
GCCCTYTCTG CACAGGAGCC AGACCGAGAA ACTCAACTGA CCAGCAGGCG GATGTGGGGT 900
GTGGGGCAGG GCATGGAGGG AGAGGAATAA AGAGAAACAG AGTCCAGGAA AAAAAAAAAA 960
10 AAAAAAATC GA 972

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(2) INFORMATION FOR SEQ ID NO: 42:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 1536 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

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GGCAGAGGCC AACTTAGTTT GAGTCTTCT TCTGGACTCT GTATGTCTTT GTGTGTACCC 60
TATGCCGTTT ACAGTCCGTA CTCTCTCTGT GARATTGGCT GTCTAATCCA GGTGGATCAG 120
30 GAGGTGCTTT GTGGTTTTTT TGCAAAGAAA TGAAGTCTGG CAAGCAAACA ATGATTAAAC 180
ATGTTTCGAT TCGTGACTTG TCTTTTGGCG AAATGCAAAG GTGGGTGTGC ATTCTTGAAT 240
TCAAAGAAAA TCTCTTTCAA ATCCCCCTCAT CCCTTGTTCG TCTTCTAAAT ACTCTCTTTC 300
35 TAGATATCTT GCACCCCCAA AACTCCCTCA GCCCCCATGG CAGCTTTTCT CTCTCCTCTC 360
TCTCTTCCC GCCTCTCCCT GTCTCCTCAC TTCAGCCTTT CCTCTTCTTT AGATCTTTAT 420
40 TATGTAGATA AAAACCCCTC CAACCTCCTT AGCCTTCTCT CCATTGCATC CCCTACCCGA 480
ATTATCTCTA AGAAAGAGGC CAGGATCCGA CACAGCGATC AGAAATCCTC CTCCCTTASA 540
AGCSCAGGGG TGAGGGAGTT CAGGAATATT CATACACTGG TAATCCTTGT CCCTGTTACA 600
45 GTCACITCCT TGTATCAGGA CCCTTGTTAC TATTTACAGA CTATTTTCCA TCTCTCTTAA 660
TGCAATTGCT CAAAGGGCAC TTAAAGNATA ATCATTATCC AITGATGTTT TTTGGAGGCT 720
50 TTTATTCCTT CCAATAAGTT CTGCCGAATA CTGGCCGCTG GCTCTATTTG TTAAACAATG 780
GAGGGCTTTG TTCCGCTTTT TTTTTTTTTT TTWTCWTAA CCTGAGCTTT CTGCCACCC 840
TTAGTATGGG GCCAAAGGGA AGATTTTTAT GCCACCCCTT TTGGTGAGAA GAGTCACTTC 900
55 CTGATTAGTG TTTGGGCTGA AAATGGGTCC CCCTTTGGGA AGAAACATGG GTGCAGTGTA 960
CTTCCTGTGT CACAGGATTA ACAGCTCCTG CCCCCTCCC AAGGAGGCAG CTCYTGGGG 1020
60 CAGTTCYTCT TTGAGAATTT CATGGTCATT AAGAAGCAGG YTCCCAGGGA CCCAGAGTG 1080

5 GGAACCTTTG ACTGAAGTCA CCACAGTGGG TGTAAGATAA ACATAAGAGA CTTTCTCAG 1140
 GGAAGATTTG GAACGAAGAA AAAGAGTAAA AAGTCACAT GGAACCATGGA GTGTTMTGGA 1200
 AAAGGGCCCA GAAAGGGAAG CTGTGGCTAA GAAGATAAAC TGCCTGATTG CAGAGACCCA 1260
 GGAGAGGGGA TGAATCTCT TTGTCTGGTC ACATTTCTCW WTAATGATKY TCCACATGTA 1320
 10 CAAAGCTAGC CAGTTTACCA AGTGCTTCCA CACACATGC TTCATTCTGT GTCTCTTAAG 1380
 CAGATTGACT CCTTGGAAAA GCCTCACGTC TGGCATCTG CACCTGCCA TCACCAGTTT 1440
 GGCTTGCTG TGCTTGGCTG GTTGGGTCTC CCCATGGTGA GCTCCCATGG TATCTCTCT 1500
 15 TCACCTTTAT ATCACTCATT AGACACCGGT GACAAC 1536

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(2) INFORMATION FOR SEQ ID NO: 43:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 2541 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

AATTCGGCAC GAGGTTCTG GCCAACCTGC TGCTGGAGGA GGATAACAAG TTTTGTGCAG 60
 ATTGCCAGTC TAAAGGGCCG CGATGGGCTT CTTGGAACAT TGGTGTGTTC ATCTGCATTC 120
 35 GATGTGCTSG AATCCACAGG AATCTGGGGG TGCACATATC CAGGGTAAAG TCAGTTAACC 180
 TCGACCACTG GACTCAAGTA CAGATTCACT GCATGCAAGW GATGGGAAAT GGAAAGGCAA 240
 ACCGACTTTA TGAAGCCTAT CTTCTGAGA CCTTTCGGCG ACCTCAGATA GACCCAGCTG 300
 40 TTGAAGGATT TATTCGAGAC AAWTATGAGA AGAAGAAATA CATGGACCGA AGTCTGGGAC 360
 ATCAATGCCT TTAGGAAAGA AAAAGATGAC AAGTGAAAA GAGGGAGCGA ACCAGTTCCA 420
 45 GAAAAAAAT TGGAACCTGT TGTTTTGTAG AAGGTGAAAA TGCCACAGAA AAAAGAAGAC 480
 CCACAGCTAC CTCGGAAAG CTCCCGAAA TCCACAGCGC CTGTCATGGA TTGTGTGGGC 540
 CTTGATGCTC CTGTGGCCTG CTCCATTGCA AATAGTAAGA CCAGCAATAC CCTAGAGAAG 600
 50 GATTTAGATC TGTGGCCTC TGTTCATCC CCTTCTTCTT CGGGTTCCAG AAAGGTTGTA 660
 GGTTCATGTC CAACTGCAGG GAGTGCCGGC TCTGTTCTG AAAATCTGAA CCTGTTCCG 720
 55 GAGCCAGGGA GCAAATCAGA AGAAATAGGC AAGAAACAGC TCTCTAAAGA CTCCATTCTT 780
 TCACTGTATG GATCCAGAC GCTCAAATG CCTACTCAAG CAATGTTTAT GGCTCCCGCT 840
 CAGATGGCAT ATCCACAGC CTACCCAGC TTCCCGGGG TTACACCTCC TAACAGCATA 900
 60

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|----|---|------|
| | ATGGGGAGCA TGATGCCTCC ACCAGTAGGC ATGGTTGCTC AGCCAGGAGC TTCTGGGATG | 960 |
| | GTGCCCCCA TGGCCATGCC TGCAGGCTAT ATGGGTGGCA TGCAGCATC AATGATGGGT | 1020 |
| 5 | GTGCCGAATG GAATGATGAC CACCCAGCAG GCTGGCTACA TGGCAGGCAT GGCAGCTATG | 1080 |
| | CCCCAGACTG TGTATGGGGT CCAGCCAGCT CAGCAGCTGC AATGGAACCT TACTCAGATG | 1140 |
| 10 | ACCCAGCAGA TGGCTGGGAT GAACTTCTAT GGAGCCAATG GCATGATGAA CTATGGACAG | 1200 |
| | TCAATGAGTG GCGGAAATGG ACAGGCAGCA AATCAGACTC TCAGTCCTCA GATGTGGAAA | 1260 |
| | TAAAAACAAA ACACCTGTAT GGCTGCCATT CTCTTCAGCC CTCGCTCTCC CCTTTCCACA | 1320 |
| 15 | GCCTCCACCC CTGACCCCCA TCTCTTTTC CTACCTCTCT GTTTGGTTTA GAAATTGCTC | 1380 |
| | AATAAGTCAT TTGGGGTTTG GCATCCTGCC CAGCCACTTC CCAAACATGA AGACCTCTCT | 1440 |
| 20 | GTGTCTTTAT GTGTACATG CCCCATAGCC ATCCCAACGT CCTCCCAGT CCTCTCCTGG | 1500 |
| | CACCAGCACC TTAGAAGTTG TTGGCAGAAG GCACCTAAAC TGTGGGAGAA GTGTGCACAC | 1560 |
| | CTTTGAGTCC CTTCCTCAA GGTAAAGCT CCTGTCAGAC TCTCAGAAGG GTCTGTGGGT | 1620 |
| 25 | GTGTATATT AGGCAAACAG GGGAAAGCTT AGAGGTCTTT CTATATGTGT TAATAAGCTG | 1680 |
| | TTTCTAAGTG TTTAAATTG AAAAGCATCA TGTCTCATG ATTTATGGGA ATGAAGCAAG | 1740 |
| 30 | TACTGAAATC AAATTAAATA CTCCTGGGT CCTGGGTCAG TTTGACCTA GCCCTGGGGT | 1800 |
| | GAGGCAAGCC CCTCCTATG AGGATGAGCA AAAATACTAC TCTCTCGCC CTGAGTTGCT | 1860 |
| | TTCTGATCT GGGGCTCAG GACTTGCTGC TTCAGTCAGC CTTATTAGC ACCAAAGACT | 1920 |
| 35 | TTATGAAGAT CCCACACACA GACACACATC CCTTCCGCC TCCCCCTGC CTTCAGTAGG | 1980 |
| | ATCTGGCTCC GTGGCTGGAG GACCAACCCC TATAGTGGGA ATGCAGAGCT TAACGTGTAC | 2040 |
| 40 | TGCTTGTGTG TGTGCTGAG TGTGTGTGTG TGTATGAGTG TGTGTCCGC CTCCCACCT | 2100 |
| | CTCCCCATCT GCTCTGGGTA TTTTGTTTT TGTTTAGTTT TAGGTTTACA ACAGAGAGGA | 2160 |
| | ATTAATTTAT CAGCAGCTA AAAGTGTGT GTTTTCTTA TGGTTTAAAA AACGCCATGT | 2220 |
| 45 | CATTGATAAC TCCCTTCTC CCTTCCCTTC TCCCGTCTG CTGATCACTC TTTCATGCCT | 2280 |
| | GTGTATCCAG GTTGCTCTGT TTCCCCACCG TTCCAGGTG TACGAGGCAG AGGGCCGGGA | 2340 |
| 50 | CAGCTTTCCT CTCAGTCATT GTTCACCCA CTGAAAATT CAGACAAGAA AACTTTGCTT | 2400 |
| | AAAAGATTTC ATGTGTGGGA ACCACAGTTC CTGGCTGCCT TTCTCCTGTG TATGTGTAAG | 2460 |
| | TTCTTAATA AATATTGCAG GGAAGGACAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA | 2520 |
| 55 | AAAAAAAAA AAAAAACTCG A | 2541 |

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2418 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

| | | |
|----|--|------|
| 10 | CCCACGGGTC CGCCACGCG TCCGCCACG CGTCCGCCCA CGCGTCCGGG ACTCAGCGAA | 60 |
| | GGGTGGGCGC CGCCGAGGCC TCCTGCCGCT GCGGGGTTTC CGCGGAGTGC CGCCCGGCTC | 120 |
| | CGCTCTGCCG CCGGCGCGGC TCATGGGCAG AGTCGGCCGG GCGGGCCGGC ATTAAACTGA | 180 |
| 15 | AGAAAAGATG TCCCTGTACG ATGACCTAGG AGTGGAGACC AGTGACTCAA AAACAGAAGG | 240 |
| | CTGGTCCAAA AACTTCAAAC TTCTGCAGTC TCAGCTTCAG GTGAAGAAGG CAGCTCTCAC | 300 |
| 20 | TCAGGCCAAG AGCCAAAGGA CGAAACAAAG TACAGTCCTC GCCCCAGTCA TTGACCTGAA | 360 |
| | GCGAGGTGGC TCCTCAGATG ACCGGCAAAT TGTGGACACT CCACCGCATG TAGCAGCTGG | 420 |
| | GCTGAAGGAT CCTGTCCCA GTGGGTTTTC TGCAGGGGAA GTTCTGATTC CCTTAGCTGA | 480 |
| 25 | CGAATATGAC CCTATGTTTC CTAATGATTA TGAGAAAGTA GTGAAGCGCG CAAAGAGAGG | 540 |
| | AACGACAGAG ACAGCGGAG TGGANAAGAC AAAAGGAAAT AGAAGAAAGG GAAAAAAGGC | 600 |
| 30 | GTAAAGACAG ACATGAAGCA AGTGGGTTTG CAAGGAGACC AGATCCAGAT TCTGATGAAG | 660 |
| | ATGAAGATTA TGAGCGAGAG AGGAGGAAAA GAAGTATGGG CGGACTGCCA TTGCCCCACC | 720 |
| | CACTTCTCTG GTAGAGAAAG ACAAGAGTT ACCCCGAGAT TTTCTTTATG AAGAGGACTC | 780 |
| 35 | AAGACCTCGA TCACAGTCTT CCAAGCAGC CATTCCTCCC CCAGTGATCG AGGAACAAGA | 840 |
| | CAGACCGAGA TCTCCAACCG GACCTAGCAA CTCCTTCCTC GCTAACATGG GGGGCACGGT | 900 |
| 40 | GGCGCACAAG ATCATGCAGA AGTACGGCTT CCGGGAGGGC CAGGGTCTGG GGAAGCATGA | 960 |
| | GCAGGGCCTG AGCACTGCCT TGTCACTGGA GAAGACCAGC AAGCGTGGCG GCAAGATCAT | 1020 |
| | CGTGGGCGAC GCCACAGAGA AAGGTGTGTC CCCAGGGAAG CGTGTGACTA GAGGGAAAGG | 1080 |
| 45 | ACTGGCCCCA TCCATATCAG ACATGGCCAG TCTTGATCCT CATGTGTGAG CAGGGGGACA | 1140 |
| | ATGAGGCGTG TGGCCAGAGG GAGAGGGCTG GCCCTGCCAT CACTAGAACA CAGGCCGTCC | 1200 |
| 50 | TGTTTCATATG ATGCACTGCC ACTTCCGTTT TGTGAAACCA GGAATCCTGA GGCTCATCTT | 1260 |
| | TATTTTTCAT GAACAGACGT AGAGAGATGA AGGCTTGTGG AGGAAAAGAT GGTGAGAGAC | 1320 |
| | TTGGGCAGAA AATGAGTAGT CCTCAGGAAG AAATCTTGGT TATGTGTTTA GAGCATGAAG | 1380 |
| 55 | GACAGAGCCA TATAGTGTGG CAGTGAATAT ACCTGCTATC TCCATCTCAG AGGTGCTCTC | 1440 |
| | TACTTTTCCC TTTTGCCCTT TCAGTATAGA TGTGATTTCT GATTCTCTTA CAGATTGTTT | 1500 |
| 60 | GCTTTGCGAG ATCTGATGTT ATGTTGCAGT CTCTTGGTAA ATGATGCCTA GTTGGTGTTC | 1560 |

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|----|---|------|
| | TATTTTCATT TAATTTTAC AGTCTGTTCT GTGTTGAGGG AATTCAGGAA AGAGACAAAC | 1620 |
| 5 | ATATGTTAGC A'TTTTAATCA GGAATTAAG TTTGAGTCAG CCTAGCTGAA CTTCCTTTGC | 1680 |
| | TAAAGAAAGA AGAAAAC'TTT TCTGGCAGCC CCGTTCATGC ACAGCTTAGG GATACATCAC | 1740 |
| | GAGCCTGACA GATGCATCCA AGAAGTCAGA TTCAAATCCG CTGACTGAAA TACTTAAGTG | 1800 |
| 10 | TCCTACTAAA GTGGTCTTAC TAAGGAACAT GGTGGTGCG GGAGAGGTGG ATGAAGACTT | 1860 |
| | GGNAAGTTGA AACCAAGGAA GAATGTGAAA AATATGGCAA AGTTGGAAAA TGTGTGATAT | 1920 |
| 15 | TTGAAATTCC TGGTGCCCTT GATGATGAAG CAGTACGGAT ATTTT'TAGAA TTTGAGAGAG | 1980 |
| | TTGAATCAGC AATTAAAGCG GTTGTGACT TGAATGGGAG GTATTTTGGT GGACGGGTGG | 2040 |
| | TAAAGCATG TTTCTACAAT TTGACAAAT TCAGGGTCTT GGATTTGGCA GAACAAGTTT | 2100 |
| 20 | GATTTTAAGA ACTAGAGCAC GAGTCATCTC CGGTGATCCT TAAATGAAC'T GCAGGCTGAG | 2160 |
| | AAAAGAAGGA AAAAGGTCAC AGCCTCCATG GCTGTTGCAT ACCAAGACTC TTGGAAGGAC | 2220 |
| 25 | TTCTAAGATA TATGTTGATT GATCCCTTTT TTATTTTGTG GTTTT'TTAAT ATAGTATAAA | 2280 |
| | AATCC'TTTTA AAAAAACAAC AATCTGTGTG CCTCTCTGGT TGT'TTCTCTT TTTTATTATT | 2340 |
| | ACTCCTGAGT TGATGACATT TTTTGTTAGA TTTTCATGGTA AT'TCTCAAGT GCTTCAATGA | 2400 |
| 30 | TGCAGCATTT CTGCACT | 2418 |

35 (2) INFORMATION FOR SEQ ID NO: 45:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 1337 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

| | | |
|----|---|-----|
| 45 | TCGACCCACG CGTCCGGAGC GACCTCTCTG CTCGCTCGT CTCGTTGGTT CCGGAGGTGG | 60 |
| | CTGCGGCGGT GGGAAATGCT GGCGCGGCG GCGCGGGCA CTGGGGCCCT TTTGCTGAGG | 120 |
| 50 | GGCTCTCTAC TGGCTTCTGG CCGCGCTCCG CGCGCGCCT CCTCTGGATT GCCCCGAAAC | 180 |
| | ACCGTGGTAC TGTTGCTGCC GCAGCAGGAG GCCTGGGTGG TGGAGCGAAT GGGCCGATTG | 240 |
| | CACCGGATCC TGGAGCCTGG TTTGAACATC CTCATCCCTG TGTTAGACCG GATCCGATAT | 300 |
| 55 | GTGCAGAGTC TCAAGGAAAT TGTCAACAAC GTGCCTGAGC AGTCGGCTGT GACTCTCGAC | 360 |
| | AATGTAATCT TGCAAATCGA TGGAGTCCTT TACCTGCGCA TCATGGACCC TTACAAGGCA | 420 |
| 60 | AGCTACGGTG TGGAGGACCC TGAGTATGCC GTCACCCAGC TAGCTCAAAC AACCATGAGA | 480 |

TCAGAGCTCG GCAAACCTCTC TCTGGACAAA GTCTTCCGGG AACGGGAGTC CCTGAATGCC 540
 AGCATTGTGG ATGCCATCAA CCAAGCTGCT GACTGCTGGG GTATCCGCTG CCTCCGTTAT 600
 5 GAGATCAAGG ATATCCATGT GCCACCCCGG GTGAAAGAGT CTATGCAGAT GCAGGTGGAG 660
 GCAGAGCGGC GGAACCGGC CACAGTTCTA GAGTCTGAGG GGACCCGAGA GTCGGCCATC 720
 AATGTGGCAG AAGGGAAGAA ACAGGCCAG ATCCTGGCCT CCGAAGCAGA AAAGGCTGAA 780
 10 CAGATAAATC AGGCAGCAGG AGAGGCCAGT GCAGTTCTGG CGAAGGCCAA GGCTAAAGCT 840
 GAAGCTATTC GAATCCTGGC TGCAGCTCTG ACACAACATA ATGGAGATGC AGCAGCTTCA 900
 15 CTGACTGTGG CCGAGCAGTA TGTCAGCGCG TTCTCCAAAC TGGCCAAGGA CTCCAACACT 960
 ATCCTACTGC CTCCAACCC TGGCGATGTC ACCAGCATGG TGGCTCAGGC CATGGGTGTA 1020
 TATGGAGCCC TCACCAAAGC CCCAGTGCCA GGGACTCCAG ACTCACTCTC CAGTGGGAGC 1080
 20 AGCAGAGATG TCCAGGTAC AGATGCAAGT CTTGATGAGG AACTTGATCG AGTCAAGATG 1140
 AGTTAGTGA GCTGGGCTTG GCCAGGGAGT CTGGGGACAA GGAAGCAGAT TTTCCTGATT 1200
 25 CTGGCTCTAG CTCCCTGCC AAGATTTTGG TTTTATTTT TTTATTTGAA CTTTAGTCGT 1260
 GTAATAAACT CACCAGTGGC AAACCAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 1320
 AAAAAAAAAA AAAANN 1337
 30

(2) INFORMATION FOR SEQ ID NO: 46:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1276 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 40 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

CTCACGCGTC CGGGACGGCN GGACGCGTGG GTGCATTTGC TGAGTGTITT ACTTCCAATT 60
 45 ATGTGATTCTN ATATTACAGG NGCTGCCATG TGGTAATGAG AAGAATGTAT ATTCTGTTGT 120
 TTTGGGTGG ARTGTTCCAT AGATGTCTAT CARGTCTGTT TGATCCAGAR CTGARTTCAR 180
 50 GTCCTGGTAT CTCARTCTTT ACTGTGARTC TTCAAATGAC ATAAGAATGA CAGAAMTTGT 240
 AGTTAAGGAC AACAGRGCAW TSAAAGGCAG CAGCATAGTC CAAAATAGAC GTGTCTTCTT 300
 CCCGAAGTCA CTGTAGTGGG GGACATAAAA TTAAAGGAAC CTCTGGGTCT TACTACCTGA 360
 55 TGTGGCCAAT TGGACTAAAA CCAATAACCA TTAAGGAWA AATSSACTWA ACCACAAGCA 420
 ACTCAATTAA MAAATAGGCA AAGAACTTGA AGAGGCATTT TCCCAAAGAA GCCAACAAGC 480
 60 ATGTGAAAAG ATGCTCAACA TCATTAGACA TCAGGAAAT ACAGATCAAA ATCAAAATGA 540

5 GATACCAGTT TATACTAAGG TGGCTATAAT AAACATCATA ATAATGAAGG ACATTAACAT 600
 GTATTAGTGA GGATGTGGAG AAATGGAACC CATTTCTGGT ACGAATGTAA AATAGTGCAG 660
 CCACTGTGGA AACAGTTTG GTGGTTCCCC AGAAAGCTAA GCATAGAGTT ACCAGAGAAC 720
 CTAGCAATTT AACTTATAGG TACATACTTC AAAGGAATTG AAAACATAGA TYCTAACAGA 780
 10 TACTKGTACA GCAATATYCA TKGTTGGCWT ATTACGATA GCCAAAAGGT AAAACAACCTC 840
 AAGTGTCAT CAAAATATAA ATGTGTAAAC AATGTGGTAT ATTCCTAGAG GGAATATTA 900
 TTCAGCTTTA AAAAGGAATG AAGTACTGGT ACATGCTACA AAGGTGGATG AGCCTCAGAA 960
 15 ACATGCTGAG TGAAAGAAGC CAATGATAAA AGACCATATA TTGTATGATT CCATTATATG 1020
 AAATKTCAG RACATTCAAG TCTATAGAGA CAGAAAGTAG ATTAGTGAYT GCTTAGGGCT 1080
 20 GGCAGGGATA AGGGGKTCAT GGCTAAAGGG TATGGGTTTT TGTGTGGA GGTGAAAAAT 1140
 TTAAAACTT GKGSTGATGG TTGCACAAGC CTGTGAAGAT ACTGAAAACC ATTGAATTGT 1200
 GTGCTTTAAA TGGATGAATT GTATGGTGT TGAATATAT CCAATAAAG CTGTTTTTTA 1260
 25 AAAAAAGAAA AAAAAA 1276

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(2) INFORMATION FOR SEQ ID NO: 47:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 1282 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

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GGCACGAGAG AAAGCCAGT TTGTGGGGCA AATTAGACTA AACTCTGTGC TGGTAGAACT 60
 GCTTTCCAAG AATGCTGTCA CTGCTATAGT TTTAATGCT TCAAATCTCA ACTCNCCTCCC 120
 TCCATTGCCC ATAGCTCAAC CATGTTCCAG GAGTGTATTC CAATCAGCTT GTTTTCTCTT 180
 AACTGGTCAA AGGAATGTTG CTCATTCAAC TGCCCCAACT CACATATTAA CAATTGTTTA 240
 ACTGGGATTA GATAAAAGGA AAGCTGACTT ACAGATGAAC CAAGAGGGAG CTATTTATGC 300
 CACAGCCCCC AGCCAGTAA CTTTATGTTT CTGATCTCCT GCAAAATTTT TTTATAAAAA 360
 AAGCTTAGCC AGGAAGTAGT AGAAAGAATA AAGTAAAGAT GGTGTAAGAA ATATATGGAT 420
 AGGCAAGTTC CWNVGYTGAG ACCTTAYGAA GAATGGTGAG GTGTGGTTAA ATGGAGGAGA 480
 TAATCAGCAG ATAAGGCTC AGATGGTCMS AAACATWTAG AACTATAATG CCATCTCCAA 540
 AGTATTGCAT GCATACAAAT GACGTTCAAT CCGTTGAATA TAATGGAGAC AACTATTTC 600

AAAAATTAAG TTCTTCTWTC TTGAGCTTTA AAAGTATACA CATTTACCCM AATGAATTWA 660
 AAACATGCMC ACMAATATTT ATATCAAAAG TGTACATGAT TTCCAAAAC TGGAGTWAC 720
 5 CAAGATTTAC TTCCWTGGGT TAGTGCATAA ATTAACGTG ATACATATAT ACTATGGAAT 780
 WTTAYTCAGC AACAGAAATA AATGAGHTAT CAAACCACAG AAAGACATGG AGGAAACTTA 840
 AATCCAGGTG GMTAAGTGAW AGAAGCCAAT ATGAAAAGGC TACATTSTAT ATGATTTCOA 900
 10 ATATATGACA TTCAGGAAAA GGCAAGGCTG CAGAGACAGT AAARAGATCA GCTAGGTGCA 960
 TGKGGSTCAC GCCACTTTGG GAGGCTTGAG GCAGGKGGAT TATMTTGAAG TCAGGAGTTC 1020
 15 NAGACCAGCN TGGGCAACAT GNTGANACCC CATATNTCCT AAAAGNACNA AAATTTAACT 1080
 GGGCGTGGTG GCACGTGCCT GTANTCCAN CNACTCTGGT GGCTNAGACN GGNGAATTGC 1140
 TTGAACCCAG GAGGCAGAGG TTGCGGTGAG CCAATGATTG CACCACTGCA NTCCAGCCTG 1200
 20 GGTGGTAGAG CGAGACTCAG TCTCAACNTT NATCAAGATA GGANNGAAAT AGAANGGAAG 1260
 AAAGAGAAAA AATAAAAAATA NA 1282

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(2) INFORMATION FOR SEQ ID NO: 48:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 645 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

AAGGTAGAAA AGTACAGAAA AACTAAATT TTCATGTGTC TGTTCATG TGGCAGATTC 60
 40 TTAAATAAC TTCGACACGC TACAATAATT AAAGTTTGA AGAACATTAA GATACTTAAA 120
 AAATAAAAGC CCACAATTGA ATAACAAAA TGAACCTTGT TTTATTTTTT ATTGGCATTAA 180
 ATGTAGGTTG CCGTGGTGAA AATAGTTTGA AATACATCAC AGTAACAGTT TTGTGCAGCC 240
 45 CTAGAGATTA AAAACAGCAA AGTAAATAAG CAGGACTCTC AACGACTCAT ACTCACAGAC 300
 ATGTTTAATG TAATCCTAGC ACTTCGGGAG GCTGAGGCGG GAGGATTACT TGAGCCTAGG 360
 50 AGTTTGAGAC CAGCCTGGGC AACATAGCAA GATCCCATCT CTACAAAAAA GTGAAAAAGT 420
 TAGCTGAACA AGGCGGCATG CACATGCTAC TCCAGACGCT GAAGTGGGAA GATCACTTAA 480
 GTCCGAGAGA TCGAGGCTTC AGTGAGATAT GGCTGAGACA CTGCTCTCAG CCTGGATGAC 540
 55 AGAGTGAGAA CCTGTCTCAA ACAAGAGAAA AAAATAAATC AAATGCTATT CAAAATTCTA 600
 AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAA 645

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(2) INFORMATION FOR SEQ ID NO: 49:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1495 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

TGTGGAAC AGTAGGAAAG CAATGAAAGA AGCTGGTAAG GGAGGCGTCG CTGATTCCAG 60
 15 AGAGCTAAAG CCGATGGTAG GTGGAGATGA GGAGGTGGCC GCCCTCCAAG AATTTCACCT 120
 TCACCTCCTC TCTCTCTCTG TCTTCACTGA CTGCACCTCT TCAGGAGAAG CTTTGTGTAT 180
 CTGTATCAGC CAGACATGCT GCTCTTCTG TTTGTGTGCT TACCCATCAC TTGGATGGCA 240
 20 GAATTCTTGT CACAACTGAG ACCACCTTCT ATAAAAGTAA GCTGAAAGGA ACAGCATCCT 300
 CGTCAGTGCT CGGCAGGGGC GGGTAGGGGA TGATGGTTTT TTCCCTAAGG TAAAACTGCT 360
 25 GTTGCTCTTG TTTCTTTTT AACTGTCAGT GTTGGCTTT CATCAGAMTG AACATTTTGG 420
 TGTTCACCTT GAACTGACGG TTTGATTTTT ATCATTTTGG AAAGGTGATC ATAGCAATTC 480
 CTTTCCAACCT TGCTAAAAT CCATACTCCC CCTTTTAAA ARWATKGTTT TGCTTMCATT 540
 30 GCTKTMCWTT TSCCTTGKCT SMCTTTTTCY TCCTGPKGSC TGAARTTKTW CYTTCYTTKT 600
 TTCCTAAGST WTTTTTCAGT AGCAAACAAG GCTGTTTTCA TCAATACCCA CATTCCCAYT 660
 35 CRGKRRGRMM ATYTAGTYTT YTCCAGKTT AAKTGKGRGR KGGKGA AAAA TRATKCKGG 720
 KANGKGGAWA TKAWAWAKG KWWATGKAAA CACAAATATA TYTYTYTAMA TTCCACTTTA 780
 ATTKGGGAAA AAAGCAGCT KAAGTGGAGT GTWAAGRARR ACCTKGRRST GCTTTTCAAC 840
 40 ATGGGATATG GTCATATRG CATRGGAAC ANGATGCCTT CTATCAWAKA TGGGTCTAAT 900
 TACTYCCTAA TTTAAACAC GTATTTTTTT AAATAGCATG TTTATTTTCA AATATDATAT 960
 45 AATGGTCGSG CRTCTTAAA TAATTTTAAA CAANGTGTC CCGRGACNGC ATATAATGTT 1020
 CAAAWGKAG AGGTAAGGAC TTYCCTTTCT GTCTYCTTAA CACTTWAGTA AATRATINGA 1080
 WTTAWAGCAA GTTTGTCCAA CTGCGNCCCT GNGGNCCGCA NANGGMWGRG GAAGGGCTTT 1140
 50 TCMAACACAA ATTCGTAAAC TTTATTA AAA CATGAGATTT TTTGCCTTTT TTTTMTTAAG 1200
 CCCATCAGCT ATCCTTAATG TATTTTANAT GTGGCCCAAG ACAATTCCTC TTCCAGGATG 1260
 55 GCCTGGGGAA GCCAAAAGAT TGGANACCCC TGATTTGTAG GTTTTCAACT TTAAAATATA 1320
 TGCTATAAAA TAAGTTCATT TAAGTAGGCT AGGCATGGTG GCTCATGTNT GTAATCCTAG 1380
 CACTTAGGGG GCCCGAGGCA GAAAGATTTRM CTGAGCTCAG CAGTTTGAGA CCAGCCTGGG 1440
 60

CCAAACGGTG NAACCCGTGT TTTACTNAAA TACCCAAAAA AAAAAAAAAA AAAAA 1495

5

(2) INFORMATION FOR SEQ ID NO: 50:

(i) SEQUENCE CHARACTERISTICS:

10

- (A) LENGTH: 1630 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

15

| | | | | | | |
|----------------|------------|------------|------------|------------|-------------|------|
| GAATTCGGCA | CGAGATTATC | TGTCTTCTTC | TTACCAATTT | ATAGAACTTT | TTAGTATTGC | 60 |
| AGATAAAGTT | CCTCATCGGA | TATCTTCTCT | CCTTCTATTG | GGTACCTTTT | TATTGTCTTA | 120 |
| ATGGGGGTCT | TTTAATGACC | AGAAGTTCTT | AGTTTTAAAA | TAGTCCAGTT | TATCCATTTT | 180 |
| TAAATGTGTA | GTGCTATTG | TGTCTGCTT | GAGAGATTTT | TGCCTACTGC | AAGGTCACAA | 240 |
| AGATGTTTTT | CTCTAAAAGC | CTTTTGGTTT | TGCCCTTTTG | TTTTAGATCT | GCAGCTCATC | 300 |
| 25 TGGAAATTGAG | TGTGTGGTGT | GTGTGTGGTG | TGAGGTAGGG | GTCTTTTTTT | TCATATGGAT | 360 |
| ATCCAATTGA | CCCAGAACAG | TGTATTGAAA | AAAAAAATCT | GTCTTAGTCA | ATTGGGACTG | 420 |
| 30 CCGTAACAAA | ATACCATAAC | CTGGGTGGCT | TAGACTACAG | AAATGTAGCG | CTCACAGYTC | 480 |
| TGGAGGCTGG | AAGGCCAGGA | TCAAGACACC | AGCAGATTCT | GTGTCTNGTG | AGGACCCACT | 540 |
| TTGTGNTTCA | TAGATGTCAC | CTTCTTGCTG | TGTCCCACTG | GTGRAAGGGG | CAAACCTAGCT | 600 |
| 35 CCCTTAAACC | TCTTTTTATA | AGATCCCTAA | AACCTTTAAT | GAGGGCTCCA | CCCTAATGAT | 660 |
| CTAATCACCT | CTCAATACCT | TATCTTGGGG | GTTAAGATTT | GAACAGAGGA | ATTTGGGGGA | 720 |
| 40 GACATAGACA | TTTGAGCAT | AGCATCTTCT | TTTCTCAGT | GCACAGCAGT | GCTGCCCTCA | 780 |
| TCATCAGTCA | GGTGTCTGTA | GGTGTGTGGC | TATTTCTGGA | CTGGGCACTC | TGTCCTACTT | 840 |
| GTTGATTTCT | CTGCCCTATA | CCAATGCCAC | ACCATCTTAA | TTATTGTAAC | CATCTTAATT | 900 |
| 45 ATTTATAAAA | AGTCTTTTTT | TTTTTTTTGA | TACAGTCTCA | CTCTGTCCCC | CAGGCTGGAG | 960 |
| TGCAGAGGTA | CAGTATTGGC | TCACTGCAAC | CTCTGTCCCC | AGGCTTAAGC | AAATCTCATG | 1020 |
| 50 CCTCAGCCTC | CTGAGTAGCT | GGGATTACAT | GTGCACCACC | ACACTTGGCC | TTCTTTCTTT | 1080 |
| TCCTTCCAAY | CCATTGTTTT | TTTATTTCTT | TCCCTKGCTT | TATKGCACTG | GCTAAGATTT | 1140 |
| CCAGTGCTGA | ATAGGAGTGA | TGACAGTGGG | CACCCCTGTC | TTTCTCCCAA | CCTCAGAGGG | 1200 |
| 55 AAAAGTATCC | AATGCATTTG | TAGATATTCT | TTATCAGATT | AGCTTCCTTT | CTAGCGGCTT | 1260 |
| GTGTCTTTGC | ATTGTTTTTC | ATGAGCAAGT | GTTGAACTTT | TCACTGAGT | TTTCCAAATA | 1320 |
| 60 CTTTTTCCAT | TGAGTTTTTT | TACTTTAACC | GTCATATTGC | CAAAAGTCTG | CATTTGTTAT | 1380 |

TTCCTCCCAA ATTGCTGGGA TTATAGGCAT TAGCCACTGC ACCCAGCCAG ACTTTATAGA 1440
 AAATCTTGAT ATCTGGTCAT GGAAGTCCCC TAGCTTGGTT ATTTTMTTTT GGTACCGCTT 1500
 5 TGTCTATTTT CGGCCCTTTC CATTTCCATG TAACTTTTAG GATCAGCTTG TCAGTTCCTA 1560
 CCAAAAAAAAA AAAAAAAAAA ACTCGAGGGG GGCCCGGTAC CCAAATCGCC GGGTAGTGAT 1620
 10 CGTAACAATC 1630

15 (2) INFORMATION FOR SEQ ID NO: 51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2420 base pairs
 (B) TYPE: nucleic acid
 20 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

25 GCCAACAGTG CTCCTCATA GATGGACGAA GTGTGACCCC CCTTCAGGCT TCAGGGGGAC 60
 TGGTCCTCCT GGAGGGAGAT GCTCGCCTTG GGAATAATC ACTTTATTGG TTTTGTGAAT 120
 GATTCTGTGA CTAAGTCTAT TGTGGCTTTG CGCTTAACTC TGGTGGTGAA GGTGAGCAGG 180
 30 WGGCCGGGGG AGAGTCACGC AAATGACTTG GAGTGTTTCTAG GAAAAGGAAA ATGCACCACG 240
 AAGCCGTCAG AGGCAACTTT TTCCTGTACC TGTGAGGAGC AGTACGTGGG TACTTTCTGT 300
 35 GAAGAATACG ATGCTTGCCA GAGGAAACCT TGCCAAAACA ACGCGAGCTG TATTGATGCA 360
 AATGAAAAGC AAGATGGGAG CAATTTTACC TGTGTTTGCC TTCCTGGTTA TACTGGAGAG 420
 CTTTGCCAGT CCAAGATTGA TTACTGCATC CTAGACCCAT GCAGAAATGG AGCAACATGC 480
 40 ATTTCCAGTC TCAGTGGATT CACCTGCCAG TGTCCAGAAG GATACTTCGG ATCTGCTTGT 540
 GAAGAAAAGG TGGACCCCTG CGCCTCGTCT CCGTGCCAGA ACAACGGCAC CTGCTATGTG 600
 45 GACGGGGTAC ACTTTACCTG CAACTGCAGC CCGGGCTTCA CAGGGCCGAC CTGTGCCCAG 660
 CTTATTGACT TCTGTGCCCT CAGCCCCGTG GTCATGGCA CGTGCCGAG CGTGGGCACC 720
 AGCTACAAAT GCCTCTGTGA TCCAGGTTAC CATGGCCTCT ACTGTGAGGA GGAATATAAT 780
 50 GAGTGCCCTT CGCTCCATG CCTGAATGCA GCCACCTGCA GGGACCTCGT TAATGGCTAT 840
 GAGTGTGTGT GCCTGGCAGA ATACAAAGGA ACACACTGTG AATTGTACAA GGATCCCTGC 900
 55 GCTAACGTCA GCTGTCTGAA CGGAGCCACC TGTGACAGCG ACGGCCTGAA TGGCACGTGC 960
 ATCTGTGCAC CGGGTTTAC AGGTGAAGAG TGCGACATTG ACATAAATGA ATGTGACAGT 1020
 AACCCCTGCC ACCATGGTGG GAGCTGCCTG GACCAGCCA ATGGTTATAA CTSCCACTGC 1080
 60

CCGCATGGTT GGGTGGGAGC AACTGTGAG ATCCACCTCC AATGGAAGTC CGGGCACATG 1140
GCGGAGAGCC TCACCAACAT GCCACGGCAC TCCCTCTACA TCATCATTGG AGCCCTCTGC 1200
5 GTGGCCTTCA TCCTTATGCT GATCATCTCG ATCGTGGGGA TTTGCCGCAT CAGCCGCATT 1260
GAATACCAGG GTTCTTCCAG GCCAGCCTAT RAGGAGTTCT ACAACTGCCG CAGCATCGAC 1320
10 AGCGAGTTCA GCAATGCCAT TGCATCCATC CGGCATGCCA GGTTCGGAAA GAAATCCCGG 1380
CCTGCAATGT ATGATGTGAG CCCCATCGCC TATGAAGATT ACAGTCTGA TGACAAACCC 1440
TTGGTCACAC TGATTAAAC TAAAGATTG TAATCTTTTT TTGGATTATT TTTCAAAAAG 1500
15 ATGAGATACT AACTCATTT AAATATTTTT AAGAAWTAA AAAGCTTAAG AAATTTAAAA 1560
TGCTAGCTGC TCAAGAGTTT TCAGTAGAAT ATTTAAGAAC TAATTTTCTG CAGCTTTTAG 1620
TTTGGAAAAA ATATTTTAAA AACAAAATTT GTGNAACCTA TAGACGATGT TTTAATGTAC 1680
20 CTTCAGCTCT CTAAACTGTG TGCTTCTACT AGTGTGTGCT CTTTTCCTG TAGACACTAT 1740
CACGAGACCC AGATTAAATT CTGTGGTTGT TACAGAATAA GTCTAATCAA GGAGAAGTTT 1800
25 CTGTTTGACG TTTGAGTGCC GGCTTTCTGA GTAGAGTTAG GAAAACCACG TAACGTAGCA 1860
TATGATGTAT AATAGAGTAT ACCCGTTACT TAAAAAGAAG TCTGAAATGT TCGTTTGTG 1920
GAAAAGAAAC TAGTTAAATT TACTATTCCT AACCCGAATG AAATTAGCCT TTGCCTTATT 1980
30 CTGTGCATGG GTAAGTAACT TATTTCTGCA CTGTTTGTGT GAACTTTGTG GAAACATTCT 2040
TTCCAGTTTG TTTTGTTCAT TTTCGTAACA GTCGTGGAAC TAGGCCTCAA AAACATACGT 2100
35 AACGAAAAGG CCTAGCGAGG CAAATCTGA TTGATTGAA TCTATATTTT TCTTTAAAAA 2160
GTCAGGGTT CTATATTGTR AGTAAATTAA ATTTACATTT GAGTTGTTTG TTGCTAAGAG 2220
GTAGTAAATG TAAGAGAGTA CTGGTTCCTT CAGTAGTGAG TATTTCTCAT AGTGCAGCTT 2280
40 TATTTATCTC CAGGATGTTT TTGTGGCTGT ATTTGATTGA TATGTGCTTC TTCTGATTCT 2340
TGCTAATTTT CAACCATATT GAATAAATGT GATCAAGTCA AAAAAAAAAA AAAAAAAAAA 2400
45 AACTCGAGGG GGGGTCCCGT 2420

50 (2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1172 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

60 AAAATTATTC TGTACCATCA CAGCTTTTCA CAACGATGGC AAGCCTTATG TCTTGGGAGC 60

| | | |
|----|--|------|
| | CTGTTTGTCT AGGCAAAGTT CAAGTGACC TAATGGGAGC TCAAATGTGT GTGTGTCTCT | 120 |
| 5 | CTGTGTGTTT GTGTGTGTGT GTGCACTCAA GACCTCTAAC AGCCTCGAAG CCTGGGGTGG | 180 |
| | CATCCCGGCC TTGCCATTAG CATGCCTCAT GCATCATCAG ATGACAAGGA CAACCCTCAT | 240 |
| | GACGAAGCAA CATGAATTAG GGGGCCCTCTT GGCCTTGGTC CAAAATTGTC AATCAGAAAT | 300 |
| 10 | GAACATAAAG GACTCCAGAG CAGTGGGACT GTCTGTCAAA AGACTCTGTA TATCTTTTGT | 360 |
| | GGATGAGTTT TGTGAGAGAA CAGAGAGACC ATTGTACCTG GCACAAGGGC TSTTCATGAA | 420 |
| 15 | AAGGGAGACT TACTGGGAGG TGCAAGACAG TGGCATTTCT CCTCTCCTCT TGCTGCTCAG | 480 |
| | CACAGCCCTG GATTGCAGCC CCGAGGCTGA GACCAGACAA AGCCCGGGAG GCAGAAAGAT | 540 |
| | GCTCCAAGAA CCAACACTAT CAATGTCTTT GCAAATCCTC ACAGGATTCC TGTGGGTCCA | 600 |
| 20 | GCTTTGGAAC TGGGAAACCT TTCTTCGGAT CCGCACTCAT TCCACTGATG CCAGCTGCC | 660 |
| | CTGAAGGATG CCAGTACTGT GGTGTGTGAG TCTCAGCAGC CGCCACACG CTCCTAACTC | 720 |
| 25 | TGCTGCATGG CAGATGCCTA GGTGGAAATA GCAAAAACAA GCGCCAGGCT GGGGCCAGGG | 780 |
| | CCAGAGGGGA AGGCCCTGGA TTCTCACTCA TGTGAGATCT TGAATCTCTT TCTTTGTTCT | 840 |
| | GTTTGTTTAG TTAGTATCAT CTGGTAAAT AGTTAAAAA CAACAAAAA CTCTGTATCT | 900 |
| 30 | GTTTCTAGCA TGTGCTGCAT TGACTCTATT AATCACATTT CAAATTCACC CTACATTCCT | 960 |
| | CTCCTCTTCA CTAGCCTCTC TGAAGGTGTC CTGGCCAGCC CTGGAGAAGC ACTGGTGTCT | 1020 |
| 35 | GCAGACCCCC TCAGTTCCTG TGCCTCAGCC CACAGGCCAC TGTGATAATG GTCTGTTTAG | 1080 |
| | CACTTCTGTA TTTATTGTAA GAATGATTAT AATGAAGATA CACACTRTAA CTACAAGAAA | 1140 |
| | TTATAAATGT TTTTCACATC AAAAAAAAAA AA | 1172 |
| 40 | | |

(2) INFORMATION FOR SEQ ID NO: 53:

- 45 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1589 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

| | | |
|----|--|-----|
| | CCCACGCGTC CGCCACGCG TCCGCCACG CGTCCGTTTC AAAGGGAGCG CACTTCCGCT | 60 |
| 55 | GCCCTTTCTT TCGCCAGCCT TACGGGCCCC AACCTCTGTG TGAAGGTGC AGTACCTAAG | 120 |
| | CCGAGCGGG GTAGAGGCGG GCCGCGACCC CCTTCTGACC TCCAGTGCCG CCGGCCTCAA | 180 |
| 60 | GATCAGACAT GGCCAGAAC TTGAAGGACT TGGCGGGACG GCTGCCCGCC GGGCCCCGGG | 240 |

GCATGGGCAC GGCCTGAAG CTGTTGCTGG GGGCCGGCGC CGTGGCCTAC GGTGTGCGCG 300

AATCTGTGTT CACCGTGGA GCGGGGCACA GATCCATCTT CTTCAATCGG ATCGGTGGAG 360

5 TGCAGCAGGA CACTATCCTG GCCGAGGGCC TTCACATCAG GATCCCTTGG TTCCAGTACC 420

CCATTATCTA TGACATTGCG GCCAGACCTC GAAAAATCTC CTCCCCTACA GGCTCCAAAG 480

10 ACCTACAGAT GGTGAATATC TCCCTGCGAG TGTGTGCTCG ACCCAATGCT CAGGAGCTTC 540

CTAGCATGTA CCAGCGCCTA GGGCTGGACT ACGAGGAACG AGTGTGCGG TCCATTGTCA 600

ACGAGGTGCT CAAGAGTGTG GTGGCCAAGT TCAATGCCTC ACAGCTGATC ACCCAGCGGG 660

15 CCCAGGTATC CCGTTGATC CGCCGGGAGC TGACAGAGAG GGCCAAGGAC TTCAGCCTCA 720

TCTTGATGA TGTGGCCATC ACAGAGCTGA GCTTTAGCCG AGAGTACACA GCTGCTGTAG 780

AAGCCAAACA AGTGGCCAG CAGGAGGCC AGCGGGCCMA ATTCTTGGTA GAAAAAGCAA 840

20 AGCAGGAACA GCGGCAGAAA ATTGTGCAGG CCGAGGTGA GGCCGAGGCT GCCAAGATGC 900

TTGAGAAGC ACTGAGCAAG AACCTGGCT ACATCAAAT TCGCAAGATT CGAGCAGCCC 960

25 AGAATATCTC CAAGACGATC GCCACATCAC AGAATCGTAT CTATCTCACA GCTGACAACC 1020

TTGTGCTGAA CCTACAGGAT GAAAGTTTCA CCAGGGGAAG TGACAGCCTC ATCAAGGGTA 1080

AGAAATGAGC CTAGTCACCA AGAACTCCAC CCCCAGAGGA AGTGGATCTG CTTCTCCAGT 1140

30 TTTTGAGGAG CCAGCCAGGG GTCCAGCACA GCCCTACCCC GCCCCAGTAT CATGCGATGG 1200

TCCCCACAC CGGTTCCCTG AACCCCTCTT GGATTAAGGA AGACTGAAGA CTAGCCCCTT 1260

35 TTCTGGGGAA TTACTTTCTT CCTCCCTGTG TTAAGTGGG CTGTTGGGA CAGTGCCTGA 1320

TTTCTCAGTG ATTTCCTACA GTGTGTTC CTCCCTCAAG GCTGGGAGGA GATAAACACC 1380

AACCCAGGAA TTCTCAATAA ATTTTATTA CTTAACCTGA AGTCAAGGCT TCACGTGTTT 1440

40 ATGAATGGG TAACTGGCAG CAAGCATGCG CACGTTTACA TGTGCGCTCC TGGTCTGTG 1500

TTTGTGTGTG CCAGCAGGG GCGCAAAGA ATCTGGCTGG GGCGGCTAAN GGAAGCAAG 1560

45 GCCTGGGCTC CGAAACANGA CCCAAGTGG 1589

50 (2) INFORMATION FOR SEQ ID NO: 54:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2074 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

60 CCGCCTGACC GCGCGGGCT TAAGGAGCC TGGCTAGGCC GGCAGCCGA TGGTCCCGCA 60

| | | |
|----|--|------|
| | GCTCGGGGCC GGCCATGCTT CGCGGTCCGT GCGCCAGCT TTGGTCTTTT YTCCTGCTGC | 120 |
| 5 | TGCTCCCGGG CGCGCCTGAG CCCCGCGGCG CCTCCAGGCC GTGGGAGGGA ACCGACGAGC | 180 |
| | CGGGCTCGGC CTGGGCCTGG CCGGGCTTCC AGCGCCTGCA GGAGCAGCTC AGGGCGGCGG | 240 |
| | GTGCCCTCTC CAAGCGGTAC TGGACGCTCT TCAGCTGCCA GGTGTGGCCC GACGACTGTG | 300 |
| 10 | ACGAGGACGA GGARGCAGCC ACGGGGCCCC TGGGCTGGCG CCTTCCTCTG TTGGGCCAGC | 360 |
| | GGTACCTGGA COTCCTGACC ACGTGGTACT GCAGCTTCAA AGACTGCTGC COTAGAGGGG | 420 |
| 15 | ATTGCAGAAT CTCCAACAAC TTTACAGGCT TAGAGTGGGA CCTGAATGTG CGGCTGCATG | 480 |
| | GCCAGCATTT GGTCCAGCAG CTGGTCTTAA GAACAGTGAG GGGCTACTTA GAGACGCCCC | 540 |
| | AGCCAGAAAA GGCCCTTGCT CTGTCGTTC ACGGCTGGTC TGGCACAGGC AAGAACTTCG | 600 |
| 20 | TGGCACGGAT GCTGGTGGAG AACCTGTATC GGGACGGGCT GATGAGTGAC TGTGTCAGGA | 660 |
| | TGTTTCATCGC CACGTTCAC TTTCTCACC CCAAATATGT GGACCTGTAC AAGGAGCAGC | 720 |
| 25 | TGATGAGCCA GATCCGGGAG ACGCAGCAGC TCTGCCACCA GACCCTGTTC ATCTTCGATG | 780 |
| | AAGCGGAGAA GCTGCACCCA GGGCTGCTGG AGGTCTCTGG GCCACACTTA GAACGCCGGG | 840 |
| | CCCCTGANGG CCACAGGGCT GAGTCTCCAT GGACTATCTT TCTGTTTCTC AGTAATCTCA | 900 |
| 30 | GGGGCGATAT AATCAATGAG GTGGTCTTAA AGTTGCTCAA GGCTGGATGG TCCCGGGAAG | 960 |
| | AAATTACGAT GGAACACCTG GAGCCCCACC TCCAGGCGGA GATTGTGGAG ACCATAGACA | 1020 |
| 35 | ATGGCTTTGG CCACAGCCGT CTTGTGAAGG AAAACCTGAT TGACTIONT ATCCCCTTCC | 1080 |
| | TGCCTTTGGA GTACCGTCAC GTGAGGCTGT GTGCACGGGA TGCCTTCCTG AGCCAGGAGC | 1140 |
| | TCCTGTATAA AGAAGAGACA CTGGATGAAA TAGCCAGAT GATGGTGTAT GTCCCCAAGG | 1200 |
| 40 | AGGAACAACCT CTTTTCTTCC CAGGGCTGCA AGTCTATTTC CCAGAGGATT AACTACTTCC | 1260 |
| | TGTCATGAAG GCTAGAGGAA GACTTCCTGG AACTGCCTTT CTTCCTACTA CAGGACCCTG | 1320 |
| 45 | GGACCTGTAG GAGCACCCCG TTTGGGACTG TGAGGTGTTT GAGGGTGTGG ACTGGCATCC | 1380 |
| | AGCAGCCACT AACAAACACA CAACTGGTGT GTAAAAGGCA GGCCTTACAT TAGAAGCCAA | 1440 |
| | GCCAATCCTT TTTCTTTTTT TTGGAGGTCC CACCGAGATA GATAGGAACT TGGATTGCTG | 1500 |
| 50 | AATTCAAAAA CAGAGCCCAT TCTTAAGATC ACTTGGTGCC TTAAAGACAC GCATTCCAAA | 1560 |
| | GTGGAATGTG GTTGAAGAAA GTGGGCCAGG TGGTTGAAGA AAGCCATGTG GGAGCTCAGC | 1620 |
| 55 | AAATCCCAAG GGCTTATTAT GACACTCCAG ATGGTCTCCT TAGCATCTCA GCTCTTCTGC | 1680 |
| | AAGGAAGAGC TTGGGTGTTA GGCCTCAGAG GCTGTAGGGT CCTTGGGTTA CAGAGCCGGG | 1740 |
| | GAGAACGAAG TTCTGTGACC CAGGGGTGGA GAATACACTC TAGGTTTGCG GGCTGGTGGG | 1800 |
| 60 | CTTTCAAATT GGTACTTCCA GAGGAAAGCC AAGCTGCTTC TGTGTGAGC GAATCAGCCA | 1860 |

AGAGCCTGAG GCTGAAGGGA AAAGTACACA GAGGAAGATA TTTTACAAAC CAGGTCAGTG 1920
TAGGCCAAGA CTTATGGTCT ACAGATTTTG GCGGGGGAGG GGGGACCTTT TCAAAGACAA 1980
TAGGGGGTCT TGACATGTTT GTTGATGTGA AAGATGATAA GATTAAAATT TTTGATTTTC 2040
CTAAAAAAAA AAAAAAAAAA AAAAAAAAAA TTNC 2074

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(2) INFORMATION FOR SEQ ID NO: 55:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1483 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

GAATCGSCA CGMCGGTGGA GCGCCACGT CCCTTGCGGC GCGGGGAGAG AAATCGCTTG 60
GACTTCGGGG CGGCCTCGGA CGGCCATGGC CTTTACCTTG TACTCACTGC TGCAGGCASC 120
CCTGCTCTGC GTCAACGCCA TCGCAGTGCT GCACGAGGAG CGATTCTCTCA AGAACATTGG 180
CTGGGAACA GACCAGGGAA TTGGTGGATT TGGAGAAGAG CCGGAATTA AATCACAGCT 240
AATGAACCTT ATTCGATCTG TAAGAACCGT GATGAGAGTG CCATTGATAA TAGTAAACTC 300
AATTGCAATT GTGTACTTT TATTATTTGG ATGAATATCA GTGGAGAAAA TGGAGACTCA 360
GAAGAGGACA TGCCAGTAGA AGTTATTACT TTGGTCATTA TTGGAATATT TATATCTTAG 420
CTGGCTGACC TTGCATTGT CAAAAATGTA AAGCTGAAAA TAAAACCAGG GTTCTATTT 480
ATCTGTTTTT TTTTAAATG TTGCACTGT AGTTTCATTA CAAAAGATCA GATCATGAAA 540
GGCAGTAACT CTCCAGGACT GGAATATCTG ATGCTCAGT GTTAATAGTA GTTCATGCTG 600
TGGTGAGATT GTTAAAAGG TGCAAGACTG TTGCTTCTCT TTTTITAGAT ATTTTCTAT 660
CTCTCACTTC TCAGGGATGA AATTCTTTTT CAAAGTTTGG AAGTTCCTTG CAACTTAGCC 720
ATGATGTGAG TGGTTATCCC TAGATAAAAT TAAAAGGATT TTTAAAAAGT AATTACTGCA 780
CATAAAATGA TAAATAGGTA ATTTGAATAA TTTTATTTTA AGCTCCTTGG TTAATTATTT 840
TGCTATTGT CTCAGCTATA AATTCAAATT TATACATACT ATTGAGTATT AATATTCTCT 900
GATTTTCAGG AGAATTCTGT CAGTCACATG ATGATTATGT TTTTNTTTAA CATCTTTCC 960
ATGCACTGT TATTTTATTA ATTTGCCTGA ATGATGAGAC CAGACCAGTG TCTACAGATT 1020
TTCATTGTCA GAAAAATCTA TAAGTCTGCC CTTTTTACAA TGATGGATTT AAAAAAACA 1080
ACAGCGTAAA TATTAGCCCA CAAGAGCAGT CCTAAACAAT CACAATTACA CTGTACTACC 1140

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CAAGAAGACT GTTTATTGTG AAGCATTAC CTTTCAAAAA ATCATTACAT TTCTATTTCT 1200
 TGGTGGAGCA GCACATTGTG GAGTGTGATT CTTAATTCCTT CATTGAGTTT GTC ATAGGA 1260
 5 CATTGATGCT GGATAGGTG TCTTTTGTTC TTATGTCTCA GACCATCTTG TGAGATTGTT 1320
 TGCCTATCTC ATAATACAGT TTTATGCAGA AAGGTTGAAA CTATGTAAAT GGTTTTATG 1380
 GAAATTATCA GTTACAATAT TTTAAAGGTG TAGAATGGCA TCTTTGTTA TAGGAGAACA 1440
 10 TTTGTAAATA AAGTTAAATT TCTAAGTCAA AAAAAAAAAA AAA 1483

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(2) INFORMATION FOR SEQ ID NO: 56:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 1123 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

CAAAAATAAT AATAGTCATC ACATTGTAT AGCACTGGGT CATTTTCCC AAGACCATT 60
 AGTACTTGA CCTCAGCTGT TGTCCAGCTT CCAGTCTGG GGTAAATGGCA GCTTAATAAT 120
 30 CTGAAATTG CCAAGAGAAA GATGTGGAAG GATGAAATGG AGGCAACATG AATTCTCTG 180
 ACCTTGTCAT ATGTTCTCAT TTCCAAGCCT TGNAGCAAG AGAGTTAGGT ATATCTTCTG 240
 TAACTCAGAC AATTTCTTC CTCTTGCGAG AATGGCCCT AGGAATCAAG GTAGCTTTTC 300
 35 TTTTGAAAC TTCATGCTGT TTTAGTGT GATAGAAAG AGGTATCTGC CATTCTCTG 360
 ACCTATTTTA TTTGTTGTA GCACCCATAA TAGATCAGCT GTCACAGCCA CAAATCTCTG 420
 40 AGGAGACTGG AATCATTTCC AGATAAATCA GAAAGTCAGA ATCACTTTAT GGTATAGTC 480
 CTGGCTTCTT GAGAGCTTGT CTGGAGGTTG TAGCAGGGA GCACAGCTAG TCATATACCC 540
 TWGACTARSG ACCGGTCTWC CTCTATTGGG GATGGTTGTC CTCTTCTACT GAGCTTGCG 600
 45 CTTTGGGAGG GACGCACATG GAGTGGTGAG GGAGGAAGGG GACACCCGCC TAGCCAGCCA 660
 GATCAGCTGA ATCAACCTG GCAATCAATG GGTGACAGA TGTGCGAGCC AGATCGCCCT 720
 50 CACATCCAGT CCTACCTTCT TGGTAACAAA ACAATTGGTT TTGCTGGTCT AGAACTGTA 780
 GGGCTAGACA TGTATTATAG GACTGGCTTA GGGAGAGTTA CTTTATATTA GCACTCATGT 840
 TTTCACTCAT TTATTCTTG TAGCTCATT AAAGAAAAAC CATAATTGAG CATCTACTAT 900
 55 ATGCCATGCA TTGTGCTGAG TATCCATGAT GCTCAGGTGA ACGGACATG GTCCTGTAAA 960
 AAGTGTAAG TCTGCTGGGA AAGTTAGTGC TCAAAAGTGT AACTAAATAC TTGAGGCAAG 1020
 60 TGCTTTACTA GGAATAAAC TAAATATCAA GAGAACAAAG ATAAGCAATT CCTTCAGAT 1080

GTTTTACATG GTAAATCCAT ACAATTTTAA AAAAAAAAAA AAA

1123

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(2) INFORMATION FOR SEQ ID NO: 57:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1239 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

| | |
|---|------|
| GTATTGATAC GAATTTTGAC TACATTTCTG ATGGTGTGTT TTGCTGGTTT TAACTTAAAA | 60 |
| GAAAAGATAT TTATTTCTTT TGCATGGCTT CCAAAGGCCA CAGTTCAGGC TGCAATAGGA | 120 |
| TCTGTGGCTT TGGACACAGC AAGGTSACAT GGAGAGAAAC AATTAGAAGA CTATGGAATG | 180 |
| GATGTGTTGA CAGTGGCATT TTTGTCCATC CTCATCACAG CCCCATTGG AAGTCTGCTT | 240 |
| ATTGGTTTAC TGGGCCCCAG GCTTCTGCAG AAAGTTGAAC ATCAAAATAA AGATGAAGAA | 300 |
| GTTCAAGGAG AGACTTCTGT GCAAGTTTAG AGGTGAAAAG AGAGAGTGCT GAACATAATG | 360 |
| TTTAGAAAGC TGCTACTTTT TTCAAGATGC ATATTGAAAT ATGTNAWGTT TAAGCTTAAA | 420 |
| ATGTAATAGA ACCAAAAGTG TAGCTGTTTC TTAAACAGC ATTTTGTAGCC CTNGCTCTTT | 480 |
| CCATGTGGGT GGTAAATGATC TATATCACCA ACCTKAATCT CTCTGCCTTT TTTTCAAAC | 540 |
| ACCCCTTCAT CATCCATCTT AATTGTCATA AGGACATATC TACTTTAATG TACTACCACA | 600 |
| GTTTACAGTT AATGTGGGAA AGACCAGCTT CAGTATCCTC TTCAGCTAGG ATTGCCCTAA | 660 |
| CTTTTAACTT TCACAGTTTC CTGATTCATA TTTGCCCAGG CTCTGATGCC TTGAATTGGT | 720 |
| TTTGGCTCTC TTTTGTGGAT CTGTTTGTGT TGTAAACAT CATAATGCAG TCTCTCATTA | 780 |
| ATTTTACCA TCATTTACCC TGATAATCTG CCTCTCTCC ATTTCTCCTT CCCTTACTAC | 840 |
| CTTCTTTTGA ATTACTGTAA CTGATTGGTC CCACCAAAAT TTTAAAGTAC ATGAAGTATC | 900 |
| TTTCTTGGTT CATCTCTTG CCCCCTCCAG ATGTCAAAAA ACTTTATCCT GCCCCCTAGC | 960 |
| TGACCACCCA GGTTCCTTTA TTTCAAGTGC CATGTGAGT CTACCTTCCC CTAAGGAGTG | 1020 |
| CCCTAATCCA GCCCTTTTTT TGTTCCTTAT GACCCATATC TTTAGGCTCT TCCCATTCTT | 1080 |
| AGGTGGGAGA TAGGTAAGTT TCAAATCTAT GCCAGTCITA TGAATATTAC ATTAGGGTAA | 1140 |
| TGTGCTATAA TGAAGAAATA AAAAATACAG TGCTTAAAG AAAATAAAAT TCTATTTCTG | 1200 |
| TCTAAAAAAA AAAAAAAAAA CCNNGGGGGG GGCCCCGGT | 1239 |

60

(2) INFORMATION FOR SEQ ID NO: 58:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 803 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

GGCAGAGGTC AATCCAGGAC TACAAACACC TGTGCCAAGA CCTGAGCTTC TGCCAGGACC 60
TGTCATCCTC CCTCCATTGC GACAGCTCCT ACCCACCAGA TGCGGGCCTG TYTGACGACG 120
15 AGGAGCCTCC CGATGCCAGC CTGCCTCCTG ACCCGCCACC CCTTACTGTG CCCCAGACGC 180
ACAATGCCCG TGACCACTGG CTGCAGGATG CCTTCCACAT CAGCCTCTGA AGGGCTGGGG 240
20 GGCAGGGGGC ATGCACCCAT GCAAAAGGCT CAGAAACTCC CCCTCCGGCA AGCCCTCAGA 300
CTTCGGAGCC TGCGCCTTCC CCCCTACCGC CTCACCTCAC AGGAGGGCCA GGCATGTATT 360
CCTCAGAGGC GAAACTGCCA AACTCTTTCT CCTGTCTTGG GTTGGCTGGC ACTGGGGCGG 420
25 GCATCTAGGG TACAGCCTCT GCTCATGGCA CTGGGCCTCC AGTTCTTCCA CATGTGTGCA 480
CCCCAGCTT GGCCAACCTT CAGCCTTGGG GTGGGGCCCG AAGCATCTTC CCTTCCGCTT 540
30 GCGCTCTCTG GGATTGGGAT GAGTGCCTGG CTCCCATCTC CTCTCACCT TTTGTTGCTA 600
TCGGCAGCTG CTGGCTCAGG GGCATCCCAM CTCCGGGCTC TGGGTTCTC TGCCCTGGAA 660
GGGCTCCAGG ACCCGTCCCA ATAACCACCC ACGGCCAGKA RGCCAAGGCC CCGTGTCTGA 720
35 TATTTAATTT TAGGGGCCCG TCTCCAGGGC GCGTAGATAA ATAAATACAC TCAGCGTCAA 780
AAAAAAAAA AAAAAAAAAA ATT 803
40

(2) INFORMATION FOR SEQ ID NO: 59:

(i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 995 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
50 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

GATTCNGCA CGAGGNAACA GCTTTATCTT TGGTTATTC TAATGTCCAC CTAGTCCTCT 60
55 TTWACTTTYC TTGGTAGGGT TAGGGTGGCA TGGGGAAATG GGACGGTATC ATTTTGTCTT 120
TTTAACTTTT TTTTTCCTCA CCTACAGCAG CTGTTTTCAC CCTGTGGTCA GTCAGGTACT 180
60 ATATTTAGTT TGCAGTGCAC CTGCTGATCG ACCCTTGATG GCCCCAGTTG GAAGTTGTTT 240

| | | |
|----|---|-----|
| | GGGGGAAGG AAYTAGGAGA GGCCAGGSCC TCCATTTAAA CCATGTCGT AATGTCCTCT | 300 |
| | TGGAAAGAAA AAAAGATACT GTTCCAGTCA TGGTTTCCTG GTAGTTGACG TTTAAAATGG | 360 |
| 5 | GCCTCATTTA AAAATTTCAA TAATTCAGGC TAATTTTTC CCTTTATATG GTAACCCAC | 420 |
| | CAAGTTTGT CAAATGTATG ATTTTATCA TGATTAAGTT TTTAYTTCCA CATCATGTGA | 480 |
| 10 | CAACTGGCCT GGGATGGGAT ATAAGCTCAG AACACAAAGT CATTCACCTC TTAATAAAT | 540 |
| | AATTCATCT GTGGCGGGTT ATGTTATTTT TGTCAAAGA GGACACAATA TGATGCAGAA | 600 |
| | TACACCATG AAGGATTTT TGGTTTGGCA AGTTCTTATT TTTTAAATG GCTGTAAAC | 660 |
| 15 | CTAGCAGTGT TTCTGAAAT GCATACCTTA CCTGATGTC AGAGATCCGA TTTACTTCTT | 720 |
| | GATTTCCAG CAAGTGATT TGAAAACATT TAATCTAATC ATTCCCCCA CCGTCTGTC | 780 |
| 20 | AAATCAAAGG AAGTGGCATC CAGCACTAAT TTTTCATCAT TTATGAAAG ATGCCTGAGG | 840 |
| | ACCCCTAAGT ATAATCAAA ATTTTGTTA ATGTGTGTC CTGTGTAAG TTCTTTAGGA | 900 |
| | GTCTAGAAC GAACGTATG CCCACTGATC ATCAAATGCA AGTTATGAAC ATTTAATAAA | 960 |
| 25 | AATTTAAAC CAAAAAAAAA AAAAAAAAAA CTCGA | 995 |

30 (2) INFORMATION FOR SEQ ID NO: 60:

(i) SEQUENCE CHARACTERISTICS:

- 35 (A) LENGTH: 966 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

| | | |
|----|---|-----|
| 40 | GACAGTACGG TCCGAATTC CGGGTCGACC CACGCGTCCG GGAGAGGACA TGCAGTGGGC | 60 |
| | ACAGAAAGTT CAATGGAACA GATGCCACTG TGGGCACCAA GACTGTAATG ACTCTGTGTG | 120 |
| 45 | GTAGGTAGTT TTAAGGACT GCATGCCTTG GAAATGATC TTCACTTGA GAACATACTT | 180 |
| | GCCTCTAGAT ATGTTTGTCA CTCTAAGCAT CCTGAATATA ACAATAGAGA AAGATAAGTC | 240 |
| | AACCAACAGA TTTAGGGATG TGTTCCTTCA GCACATTTTG GTCATTTTGA TGCCAAGTTT | 300 |
| 50 | GACATACTGT TTAATTGGG AGCACCTTTG CTCCTTTACC AGGTATGTAT CACTTTGTTA | 360 |
| | CTCCAGGTGC CATTCCTGGT GATGACAGAA TGTATATCAC TATCGTTGTT AGCAAGAGGA | 420 |
| 55 | AGCTTTCAAT ATAGGAACCT AACATCTTCC CATGAGTATA AATGAATTTA AGACATTTGA | 480 |
| | ATCAAACTT CAGTAGAGG AGGTTTATA ATTCATAAAA CTGGTTAAG GAAATCTTT | 540 |
| | TTACTTTTCC CAAGGTTAAT CTTTTTAAAT ATCTCTAGAC ATCAAATACT TTCTGTATGT | 600 |
| 60 | ATTAGCTGTG TCTGTCTATG ATGCAAGTAA CTCTCCTCT ATTTGGGGGA TAGTTCAGAG | 660 |

AGGTAGGAGC ATTATCTCCC ATTTTCTGG TGA CTCTTG GAGTATAGAA TTCACCATTT 720
TATCCGTAAG TCTTCAAAGG ATTATGGTGG ACTAGAACTT ACATAGTACA AAATAGTCTT 780
5 CTATTTTAA TAGGAACTTA GAAAAA ACTT AGAATTATAT ATAGTGTGT TTCCTTTAGA 840
AACCAGAGCT ATTTATTTGT ATTTAAAGCA CTGTTTATTA TTTGTA CTGA TTCTTATCCC 900
10 TCTGTGTGAA TAAATGTAAG ACGGTGAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 960
ACTCGA 966

15

(2) INFORMATION FOR SEQ ID NO: 61:

(i) SEQUENCE CHARACTERISTICS:
20 (A) LENGTH: 262 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

TTGCAGGTAT ACATCCAGAT GCACAGAATG TCCATTGTG CTTATTGGT GATGCTAATT 60
TTGATCACTT GGGTAAGATG TCCAGTTTCT CCAGTGTATC GTTATTGTTT TTCCTTTTGC 120
30 AATTAGTGGG TAATTTGTGA GGAGAACTT TGAGACCTTG TTTGACAATT CTGTTCTCTC 180
ATCAAATCTA CCCCTCCCTA GGTTTAGCAT CCTTTGACAA TCCTTGTCTT GAATAAATTT 240
35 TTA ACTAAGA TGTTTNCCTA AN 262

40 (2) INFORMATION FOR SEQ ID NO: 62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 753 base pairs
(B) TYPE: nucleic acid
45 (C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:

50 GGCACAGGTT CTTTTCAGG TCATGACAGA ACCATGCAAG ATATTGTTTA CAAATTGGTA 60
CCAGGCCTCC AAGAAGGTGA GTGTCTGACT GTCTTGCTGA TCCCTGAGGT CCCAGCCTGG 120
CCTCTGCAGC CCTGCTCTC CTGGAAGTTT GGTCTCTGGA TGGGAGGCC CTTTCTTTT 180
55 GGCCGAATCA CCGTCTTCTC ATCCCTGCTC TCAGCCCAAC TTCATCTCCT TGGCTGGTCT 240
CTTCTTTTCT CTAAGATGCG TAKACATCTT TTTACCCCTT ATGTGTATTC ATTCAGCAAG 300
60 TATGGATGCG ATGTTTAGCA CATGGGAMCC CCAGGGNTCA ACGCAGCTCC TGCCCTCTCC 360

AGGACCCCTGC CTTSTTCCTG GGGCCACCT CCTGTCCCAG GCTGCCTCC CTCATCCCA 420
CAGCGCCAGC TTCCCCACAA CAGAGGAGCA GCACGTTGGC ATAGCGGGTA GCTGGTGTTC 480
5 CTAGAAAAAC TTCACCATAA AGTCAAATTT CATTTAGAAT TAAAAGAAAT ACCAAGTAGT 540
ACAAATACCC TGAAAGTGA AATCGGTTGC TTGGGGATCG CTCAGCTGAA AGCTCCCCCA 600
10 GCTCCCGACA CTCTCAGGT GGTGGCCCT CCGCTGGCGA ACCGGCAAAG AAGCCCAAGG 660
AAGGGGGCCA GGTTCAGCGC CCAGGTGGG CTGTGCCCTG GTTATTCCTG CTCCATCCAN 720
AACCTTTCCA AAAGGCAGAA TAGAAAAACN TGA 753
15

(2) INFORMATION FOR SEQ ID NO: 63:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 739 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

25

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

ACAATACATG CATCATATCT TTTGACTTTG AAGGATATCT CATGTCAAAG GAATCAAGTT 60
30 ATGATTTATA GAGGATTCAG CTGGAATACC TTGTGGGTGC TGGCTGAGGG TGGCAAAACG 120
CCTACCGAGA CATGAAGGTT TTAGCCACTA GTTTTGTCTT TGGGAGCCTG GGGTTGGCCT 180
35 TCTACCTGCC TTTGGTGGTG ACTACACCTA AAACACTGGC CATCCCTGAN GAAGCTGCAA 240
GAAGCTGTGG GGAAAGTTAT CATCAATGCC ACAACCTGTA CTGTCACTTG TGGCCTTGGC 300
TATAAGGAGG AGACCGTCTG TGAGGTGGGC CCTGATGGAG TGAGAAGGAA ATGTCAGACT 360
40 CGCGCCTTAG AATGTCTGAC CAACTGGATC TGTGGGATGC TCCATTTAC CATCTCATT 420
GGCAAGGAAT TTGAGCTTAG CTGTCTGAGT TCAGACATCT TGGAGTTTGG ACAGGAAGCT 480
45 TTCCGGTTCA CCTGKAKACT TGCTCGAGGT GTCATCTCCA CTGACGATGA GGTCTTCAAA 540
CCCTTTCAAG CCAACTCCCA CTTTGTGAAG TTAAATATG CTCAGGAGTA TGA CTCTGGG 600
ACATATCGCT GTGATGTGCA GCTGGTAAAA AACTTGAGAC TCGTCAAGAG GCTCTATTTT 660
50 GGGTTGAGGG TCCTTCCTCC TAACTGGTG AATCTGAATT TCCATCAGTC ACTTACTGAG 720
GATCAGGACT AATAGAGAA 739
55

(2) INFORMATION FOR SEQ ID NO: 64:

60

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 476 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

| | |
|--|-----|
| GAATTCGGCA CGAGAGGACA TGGATTATGG GTACTACTCA GCAGGCCAGT TTTTACTCCA | 60 |
| 10 CCTCTTTCTA GCTGACTTGA CACAAGCAAC AACCCAACAG AAAACCAATA CTTCTGAGAA | 120 |
| TGGCTGCAAG TTTGTTTGTG CTGCTTTTGT AGGTAAGAAA TCAAGGCTGA GCTCTTCTTT | 180 |
| CTCCTAATTC TCAGGAAGGA GGAAGGCAGA TGTGAGAACA CTGATTGGGT CTGAGTGTAC | 240 |
| 15 TGGGCAGCAT CACTGTTAAA AGGTCAGCAC ACAGATGCAA GCTCACTTGT CTGCTTNCCT | 300 |
| TCATGTGACT GAAGTGGTTA AGAARGTTGT NCAACTCCCC CCTGCACCCC CCTCACCACC | 360 |
| 20 GCAGTAAGGG AGAGACAGGG CCAAACCTGC AGCTTCGGTA GAAGAGGCCA AGGCAGGTGT | 420 |
| CCAAGGCCAG ATCAGCAGTC AGCCAGGGCA AATGGGCTCA CTCTGGTTAC ATGACC | 476 |

25

(2) INFORMATION FOR SEQ ID NO: 65:

(i) SEQUENCE CHARACTERISTICS:

30

- (A) LENGTH: 754 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

| | |
|--|-----|
| AATTCGGCAC GAGACCAATT GTACTTTTAT TATATCAGGC TGATTCAGT TTTCTAATGC | 60 |
| AATGAACCTG ACACAGATTT TAAATTTTCT CTCAATCTGT CCCATTGTGT AGACAAATTA | 120 |
| 40 ATTCAAAGTT CTTTTTCTTC CTCTCTTTT TCATCTAAGC CTGTGCTTAT GAGTAGAAAA | 180 |
| AGAGAAGAGG CTACCTTGAA ATGCCTCGGG CCCAACTCA GAAGGCTCTG CACTCAACTG | 240 |
| 45 AGCCTCCCTT CCTACTAAGA ATGGAATAGT GTTGCTTATA GGGGTGTTGG TCCAAGTATC | 300 |
| AGCTGTGGAT GATTAATTCC CAGGGCTGCT ATCACCTAAG GTAACCTCAG TAATCTTATG | 360 |
| TGTTTGGAAG GGAGGATGAG GATTATTTTT CAAATACATA ATTTTGTTTT ATTTTGAAAC | 420 |
| 50 AATCTCACAC CTACAGAAAA GTTGCAATTA TAATACAAAG AGCTTCCCCC TCGCCTGAAC | 480 |
| TGTTTGATAG TAAGTTTGCC AAAGTATAT ACCCAGATC CCCAAATGCT TCAGTGTAT | 540 |
| 55 TTCCTCCAG CCAAGGACAT TCTCCCTGCA TAACCCACAA TACAACCCAT AAAAGTCAGG | 600 |
| AAAATTTAAC ACCCAGTTCC ATTTTGAAC CCATCTGAA ATTCCAGGTG TTCATTCCAT | 660 |
| 60 GTTTTGGCC AGTTGGTNCC TTTGGTATGT TCCCTCCNT AGCCCAAAAA AAAAAAAAAA | 720 |

AAACNCCAAG GGGGGGGGCC CCGGTCCCA ATCC

754

5

(2) INFORMATION FOR SEQ ID NO: 66:

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 1890 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

20

| | |
|---|------|
| GGCAGAGRAA AAACAAAATG GGTAATGCAT TCGAGGTGAC AGGGTTAATG TTGGCATTAC | 60 |
| TTTGTATATGT TGTGATGGG CAGAAACCCA AGGKGGGGTT TTKTTGAGCA TAAACACAAG | 120 |
| AAGCAATTAT TTGTGGCACT AGACTTAACC CAAAGGACAG ACCCCTACAT GTATATAGTA | 180 |
| GAGAAATCCT GTCITTTAGC ACTATCTCAC AGGGGAAGCT GAGGAATCAC ATTATCTTTA | 240 |
| ATATAAATAA ATGAAATGCN AGCACTGTAT AATTTATATC CTTAAGCAAC TGGATTCAMC | 300 |
| GTACCACTAA TGGCCTGGTC ATGTTTTTAA CATTACCCCA AAACAGCCTA ACTGTTCTGT | 360 |
| GACTCAGTGT CTCTGTGGAA TCCTATTTAG TAGCACCATG GTCTCTAAAT GTTTTGATTA | 420 |
| CACATCAGTA TTAGGAAAAC ATGTTTGAAG CATTGTCTAA GTCTGTTTGT GCTGATGTAA | 480 |
| CAGAATACCA TAGACTGGGK AGTTTATAAA GAGAGAAATT ATTGGCTTAC AGTTGTGGAG | 540 |
| GCTGGAAAGT CTAGTATCAG CGTACTGGGA TTTGGCAAGG GCCTTCTTGG TGCATGATAG | 600 |
| TATGGTGGAA GGTATCACAC GGCAGGCAGA AAGGCAGAGA GAGAACAAA GGGGGCGAAC | 660 |
| CCACTCCCTT GATGAGAACC TAAATACCTC TTAAAAGTCC TAACTCTCAA TGCTGTTTAC | 720 |
| AATGGCAACC AAATTTAAAC AAGAGTTTTG TAGGGAACAA ACACTCAATC AAAACCATAG | 780 |
| CAAGTATGTA CCATGACTGT ATGTGTATTT ATAAAATACA TTCATATATT TCTACAGCAA | 840 |
| TATATATGAG GTACATTTAA GCATGTAAAA ATAGGAATTT TAAAAATAG GACAGTTGTA | 900 |
| ATAATTTCTT TGTACATTCC ACTTTGGAGA CTGTTTTTAT ATGGRGCTTG TTTTATCACC | 960 |
| AAAAGGCATT TTAATTTTGC ACACTTTAGA WTTCTTACAA TGTGTAATG ACTGCTAGTT | 1020 |
| GCTGAACAAA GGACAGATAA AGTGTTCCT GCACCTGAGC AGCCTAAAGG TGAGTGAAT | 1080 |
| ACAGATGCAC AAGTGACTGG TTGATAATGG AATGAGACCC CTTATAAGAA AGACATACAG | 1140 |
| AGCACGGCAG AGGAGCAAGA ACMACACAGA GGCAATGACA TTTGAGCTAG GCCTCTTATA | 1200 |
| TCTGTAGATG AACATTTGAT GGTAGGTAGT AGGGAAGATG GAACTAAGAA TATTTGAGCT | 1260 |
| ACTTAATATA TGCCAGGCAG CATGCTGAGT GCTTGTGTTT ATTTAATTCT CAAGACAGCC | 1320 |
| ATAAGCGGCA ATACAGGTAT TGGGCCTATT ATTCTAAATC CCATTTTATA AGAGAGTTAG | 1380 |

GATTAGATTC AGTTCCATCT TTCTACAAAA CCTGGCACTG TCATTCCAGG CAAAGGGAGT 1440
 ACAATCCATT TTTCTCTTAA GAGGTIGATT TTGCCAATGA GACAGAATGA ATCTCTACAG 1500
 5 CTGTGTTAAGT TTCWACCCGT CTTTGGGTGA CTGAAAAATT CAAATGTAAA GATGTGGCAA 1560
 AATTGGTTCT CTAAGGATTT TAAGTACAGC CAAATGATAT GTCACAAGTT TTTTCCTAAA 1620
 10 TATCCAACCA TTTAGTCTTT CATAAGCTTT TAATTCCACT AGCCTCACTT TCTGAGATTG 1680
 TTGATGTTTT CTGTCTTAA CCTGAAATTT TCTTTGTTTG ATGTTAACAG GAGTATAATG 1740
 AAGGAGTAAC CATTTTATT TTATGATAGT CTATCAATAG ACTTTTTTTA ACCTTCTTTA 1800
 15 AGCTAGGTGT GTTTGTCCTT TATTAAAGTC AGTTTGACCC AGCCTGTACA ACATGCAAG 1860
 ACCTTAACCT TAATAAAAAA AAAAAAAAAA 1890

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(2) INFORMATION FOR SEQ ID NO: 67:

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- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1614 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

AAATAAGACN TCTTTGAGCA GCGATTGCTG GATCAITGAT CTGTTTGAGG AATGTCTGAC 60
 35 CTGGGCCTRA RAGCTGGAGA AGGTGCAGAT TCAAAGTRAG CGGCTCCTRA GGAGAGCCCC 120
 AAGSTGCTCG CCTTCTCCGT GGCTTCGCA GCTACCGTCT GCACGGTGAG AGGGCACGGG 180
 CACACGGTTC GGGCTGGCGT GCAGTCTCCC AGCCAGCCAC GCTCTGCTCA GGCCTGGAAG 240
 40 TGAAAGCCGC CTCCTTCCCG TTATGCCCCC CATACAGGAG CCTCGGTTTT TCAGCAAAAC 300
 GCGGCCAGTC CCTTCTTCCA CTGCTGCCTC CCAGCAGAGG GCCCCAGGAT CTCCAAGGTC 360
 45 CCAGCTATGG CTTTGACAA CGTGGCTTCG GCCCCTGGGG TTGCAGAGCT TGCATPGGGT 420
 TTACCTCGGT CTCATTCATT CATGGAGCCA AGGGTGGGGT TTCACCTGCG AACATCAGAC 480
 TGACTTGCTG GCGTCAAGAG CAGTTGACTC ACTGATGAAG GCCCTGGTGA GGAGAAAGCA 540
 50 CTCTGTTCTT CGCCTACTCT GTAATCGTTT TGTCATAATG AGCCATGAAA AAAGTAATGA 600
 ACTTGTGCTG TTAATCGTCA CTGTAATGAG AAGTCTTACG TACAACATAG CTGTGGTGGC 660
 55 TGGGTGGTTT AATGGCTGCA TTAGATAGGA TCCTCACATC CCATTCAGAA CCAAACTGA 720
 TACAGTGAAA CAATTAAGGT GAGCAAATAG TTTTAACTTT TCTTTTTTTT TTAAAGTTTC 780
 ATTCTTCCTA GAATATTTTT CTAACAATTT TTATTTTCAGC TTAAAGATG GGTCAATATG 840
 60

CCAAACGGGC CATATAATCC AACATTGTTG AGATGTCTTA GGACATCTAA GGCAAAACTG 900
 GCACATTTGT TCTGCAGAC T ATTGCAGGAA TGTMTTMTCC TAGCATTTCT ATATTATCTG 960
 5 TCCATTCTGA GGAACCAGTG AATGTCCTAT AAATGCACCT CCTGTCAAAA CCATGCCTGA 1020
 GAGGTCCCGG CTGGGAGTGA CAGGGTGCTT NCTTAGATTC TATTGGTCCT TCTCTCATTC 1080
 TCCGAACTTA CTCCTMTTTA TGGGTAAGTC AACTAGGTYT ACAGTCCCTT ATTTTAAATG 1140
 10 CCTAAGTTTT GACAGCAGGN AAGAAAACAA TTTTAAATAA ATTCTCATTA CATAGACGCA 1200
 CAAGAATATG TCACATAAAG AAAATGTGTT TAGAATACTG GTTTTCTATT TACGCATGAT 1260
 15 ATTTTCCTAA GTAAAATTGC CAAGTGGACT TGGAGTCCA GAAAGGAAAA TAATTTAAAT 1320
 TAATGCTGGT GATCTTAACA ATATTTTGTA AAATGATGCT TCCCCCTTCT CCATGGTGTA 1380
 GTCAATTTTG TACAATTAGG TATCTGACTT TACAAGTTTG TTATCCTTTC TAATTTTAC 1440
 20 TGAAGTAAA GCACAAAGAA GACTACACAG AAAATCTGGA AACAGTTGCA GGTGTTGGGA 1500
 GGAAGATGAA ATCGAGCTGT CTMTTAACTT TCGTATGTGT TTTATCAGAA TTTGCTGGAC 1560
 25 TATGCTAGCA AGGACTTTGT TTACNATCAA ATTGTACTAG TGTCTGCAGG GTTT 1614

30 (2) INFORMATION FOR SEQ ID NO: 68:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 596 base pairs
 (B) TYPE: nucleic acid
 35 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

40 CTTTTCACCC TTAGAGACAG GGTTCACCTT TTTTGCCTTC TTAATGGAGA TATTCAGTTT 60
 TCTTTTTTTC ATTAAACAA AGAAAAAAA TGTATCTACT CTACCTTCCC TCTGCTCTCC 120
 TCCCTCCCTA TCCTACTTGC CCATATGAGC ACGGCTCCCC ATGGCCACAT ACTCCTGCAA 180
 45 AGCTTTTATG CTGCTTCGCT TTTCTCTAAA CAGATCTGAT ATTGCTGCTC CTGTGGTTTT 240
 CTCAAAATTA ACTTTGCCGT GGTMTTAA AAGGAATCAA AATGCATTGT TGCATTAAAGC 300
 50 TTTTCAATA AAGGAAATT ACGGAAGGAA AATAGGCAAC ACCAGCAAAT TATATGTGGA 360
 CAGGTTCCTAA ACTCTATATA TACATATATA TATATATATC TATATATCTA TATACGTAAT 420
 CATCTAGTTC TGTCACTCTA CTGAAAGGAA TAACACTTCT AAAGATCACC ATTTCTGAGA 480
 55 AGTTCTTGGA AATCTTTATG TCTAAGTGAT TGTATTAGAT CAGCAATAAT GACTATGTAA 540
 TCTCAAAAAA CAAATAAAAT ATTCTTAACA TGGAAAAAAA AAAAAAAA ACTCGA 596

60

(2) INFORMATION FOR SEQ ID NO: 19:

5

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1524 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

| | | |
|----|---|------|
| | ATCCGGAATT CCCGGGTGTG TTCGACCCGT CCGGGACTTT GCACAGCACC TTCCAGCCCA | 60 |
| 15 | ACATTTCCCA GGGAAACTT CAGATGTGGG TGGATGTTTT CCCAAGAGT TTGGGGCCAC | 120 |
| | CAGGCCCTCC TTTCAACATC ACACCCCGGA AAGCCAAGAA ATACTACCTG CGTGTGATCA | 180 |
| 20 | TCTGGAACAC CAAGGACGTT ATCTTGACG AGAAAAGCAT CACAGGAGAG GAAATGAGTG | 240 |
| | ACATCTACGT CAAAGGCTGG ATTCTGGCA ATGAAGAAAA CAAACAGAAA ACAGATGTCC | 300 |
| | ATTACAGATC TTTGGATGGT GAAGGGAATT TTAAC TGCG ATTTGTTTTT CCGTTTGACT | 360 |
| 25 | ACCTTCCAGC CGAACAATC TGTATCGTTG CGAAAAAGA GCATTTCTGG AGTATTGACC | 420 |
| | AAACGGAATT TCGAATCCCA CCCAGGCTGA TCATTGAGAT ATGGGACAAT GACAAGTTTT | 480 |
| | CTCTGGATGA CTACTTGGGT TTCCTAGAAC TTGACTTGCG TCACACGATC ATTCCTGCAA | 540 |
| 30 | AATCACCAGA GAAATGCAGG TTGGACATGA TTCCGGACCT CAAAGCCATG AACCCCTTA | 600 |
| | AAGCCAAGAC AGCCTCCCTC TTTGAGCAGA AGTCCATGAA AGGATGGTGG CCATGCTACG | 660 |
| 35 | CAGAGAAAAGA TGGCGCCCGC GTAATGGCTG GGAAAGTGA GATGACATTG GAAATCCTCA | 720 |
| | ACGAGAAGGA GGCGACGAG AGGCCAGCCG GGAAGGGCG GGACGAACCC AACATGAACC | 780 |
| | CCAAGCTGGA CTTACCAAAT CGACCAGAAA CCTCCTCCT CTGGTTCACC AACCCATGCA | 840 |
| 40 | AGACCATGAA GTTCATCGTG TGGCGCCGCT TTAAGTGGGT CATCATCGGC TTGCTGTCC | 900 |
| | TGCTTATCCT GCTGCTCTTC GTGGCCGTGC TCCTCTACTC TTTGCCGAAC TATTGTCAA | 960 |
| 45 | TGAAGATTGT AAAGCCAAAT GTGTAACAAA GGCAAGGCT TCATTTCAAG AGTCATCCAG | 1020 |
| | CAATGAGAGA ATCTGCTC TGTAGACCAA CATCCAGTGT GATTTTGTGT CTGAGACCAC | 1080 |
| | ACCCAGTAG CAGGTACGC CATGTCACCG AGCCCCATTG ATTCCCAGAG GGTCTTAGTC | 1140 |
| 50 | CTGAAAGTC AGGCCAACAA GCAACGTTTG CATCATGTTA TCTCTAAGT ATTAAGTT | 1200 |
| | TTATTTTCTA AAGTTAAAT CATGTTTTT AAAATATTTT TCAAGGTGGC TGGTTCCATT | 1260 |
| 55 | TAAAAATCAT CTTTTATAT GTGTCTTCGG TTCTAGACTT CAGCTTTTGG AAATGCTAA | 1320 |
| | ATAGAATTCA AAAATCTCTG CATCCTGAGG TGATATACTT CATATTTGTA ATCAACTGAA | 1380 |
| 60 | AGAGCTGTGC ATTATAAAAT CAGTTAGAAT AGTTAGAACA ATTCCTATTT ATGCCACAA | 1440 |

CCATTGCTAT ATTTTGTATG GATGTCATAA AAGTCTATTT AACCTCTGTA ATGAAACTAA 1500
ATAAAAATGT TTCACCTTTA AAAN 1524

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(2) INFORMATION FOR SEQ ID NO: 70:

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- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 819 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

GGCACCAGGG AGAGGGACGG GGAGGGGGCG AGGGGCGGAG GCCGAGGGGG CAGGGGNTGG 60
GCGGCGGCCA GTGTTTACAG ATGAGCTTTA ACTGCCGCCT CAGGCGTGA GACGAGACC 120
CCGCAGCCCG GCGGCGCCTC AGCCCTTCAA CGACAGTATT GAGTGGTCAG GTTACAATAA 180
ACCGGAGAGA AAAGTCCGC TTGCACCTTT TTTAGTTTTT TTATTTTAG ACACCCCTCC 240
CCTCCAGGT GATCTTTAAA AAAGCAAAAC AAAAAACAG ACTTTTCCAG CGCTCAGCGT 300
TTTTTCCTTT CGTCCGAAGC CGTTTCTGA TTTGACTTTT CTCGCCGCC GGTCTCAGGC 360
CCACAGACGT TCCAGAGGAG GAGGGTGACA TTTTACTCC CTTTTGGGG CTAACCATTT 420
ATGCTTTTGT ACATCAACCG TCGCGGCCG GAGGGGCGAG GGGGCGGGG GCGAGGGGCG 480
TTCCAATCAA ATTTCTAATT TCTGTTAATT ATTAATCCCC KTTTACTGC GGTTCCTGTT 540
GTCATTTTA AAATTTTTT AATTTTTTT TTTTTTTAC TTTTACTTT TACCTCTTGT 600
GTATATGTAG GGAATTTATA GGGAAATATG TACTTTATGG AATAAATTT AAGAACTAAA 660
ATATATTTTA TTTTAAATAA AGTAATGGAC CTTTAATCTT ACACAGCTAA ATTACTGATT 720
ATATATTTSC TGAGCTGATT TAAGGGTTAA AAAAATTGTA TCAAGAGTTT TATTTTTTGA 780
CTTCAAAGCC TTCTTAATAA AGCCTCTTTT CTACATGTG 819

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(2) INFORMATION FOR SEQ ID NO: 71:

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- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1442 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

AATGCTTGG CATGAGTTTA CTTTAATGGC TGTTTCTGAG TTTGATCCCT CTCCGAACC 60

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AACCSTCTG ATGTGTCCTG TTCCAGCAGG AAGAGACAGA CCTGGAGGTT CTGTACTTGT 120
 GATTTCRGTT TGTGGATCCT GAGAACAAGA AGTACTGGGA TCCTAAAGTT CTACATTTC 180
 5 CAAAGCAGAT TAATGACCTA CCACATTCCA GATCATTTGG TGAYVWTGTG TTGTGCGTGT 240
 GGGTGTGTGT GTGTGTGTGC CAAATCAAG GTGGTCCCAG CCTTCTAGT CTTCTCTAAC 300
 CTTCTTCTC ARAARTCGCA CCTGTCTGT CTTCTAGGA TATAATTTTT TTTCTATTAG 360
 10 CCTGGGTAAC ACCCCAACCA ATAAAGTTTG CAATATCCAA GCCTCCTAAT TTCTCTACTT 420
 ATTAGCTTAT ATTAAGCTTC AGCATGAGCA AGCCTAAAA CTCGCCATTA TCTGGAAAAG 480
 15 TTCTATTCA CAGGCTTTAA TCTCTCCTAG AGTAGTTAGC ACTCTTTTGT GGCTTTGTGT 540
 TCCTGTACTA GCTTGAATTC CACAGTCTGA CGTTAATAAT TAGCTCCTTA ACACGTCCAT 600
 CCTCTCTGA TGTCTGCTC TCTATTTTC CTTCTTTCTT CCAAGTTGGG ATAAATTCAG 660
 20 CTTCTTATTT TCCTGCTCCA GACCTTGGTT GTGGAGAAAG ATAGAAAAAG TTCCATACAG 720
 GGGACTCTGT GATCCTGCTA ACATCATTAT TTACCTAAGC TCTTTAGACT CCAGTGAAAG 780
 25 CTTCTGATTT AATGTCATGT CCTACTTTA TGCCACATGT CCCATACCAT TTTCTTTGTT 840
 TTATGCAATT TATTTCCACT ATCTGATCCC ATTCACCCA CATGACTTTG AGTGGAAAAC 900
 TTCATCTCTT CATTGCTGAG TAAACAACT TCAGGATGAA CAAGCCCTGT CCACTATTTT 960
 30 CCCTTTTACT KTAAARKYCT GGAATTIWWA TGATCTACGT TTTTTCCTC TGTTTTATT 1020
 CTTCACTCCA TATCAACTTA CTGGGGATC TACACCTTCA TTCATYCTTT TCATTCTGTC 1080
 35 GGCACCTGGC TATGGAGTTT ACATTCTTCA TCATATTTAC TCCTCATAAT AATCCTGTGA 1140
 GGTATATACC ACTCTGAGTC TTGTATAAGA GAAAAAGAAA CTGAGATAGG GATAACTCAA 1200
 AGGGATAATT CATTTGCTGG AGCTACCAAC TAGCTACTAA CCATGCTAGA ATGGACAGAG 1260
 40 ATGACATTCA TGCCAAAGAC CATGTTGACT TGCTATCTCT ACATTGCTC TAAGTTTAGA 1320
 AAAAAAAAT CCCTTCAATT TATCCTCCAA CAGTCTTCTT AGAACCTTAC CATGGATGCC 1380
 45 TTGTWTAACA CATTTACCT TTCTGGTAAA AAAAAAAAAA AAAAAAACTC 1440
 GA

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(2) INFORMATION FOR SEQ ID NO: 72:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1223 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

| | | |
|----|---|------|
| | AACCTGAGGA GGCTGTCATG ATAGGAGATG ATTGCAGGGA TGATGTTGGT GGGGCTCAAG | 60 |
| 5 | ATGTCGGCAT GCTGGGCATC TTAGTAAAGA CTGGGAAATA TCGAGCAACA GATGAAGAAA | 120 |
| | AAATTAATCC ACCTCCTTAC TTAACCTGTG AGAGTTTCCC TCATGCTGTG GACCACATTC | 180 |
| | TGCAGCACCT ATTGTGAAGC AATGTGTGCA TCTGAAGCAA CTTGAAATGC AGCTTCTTAT | 240 |
| 10 | TGCTCGAAT GAATCCCTTA CCAACTCAGT GCCAGCATCG GTAGACACCA GTCAGTGCTG | 300 |
| | ATCGCTTTT AACCTCTTT TGTGTGTCAT TAATTAGAAA GAAAGGTATT GAATTGCGGC | 360 |
| | TAGCCAGTAA GCCTTGCTAA TCTCTTTTAT TTTGTAAGT AAGATGAGAC CCAAGAAAAG | 420 |
| 15 | GGAAAGCTGA GATTTGTGC CATTCCTTTT AAAATATTCA TCAGTTAGG TGGGGCTGTG | 480 |
| | GGGAAAAGC TACTACAGGG AAGAGTGTTC TCTGCTGTCT CTTCACTGGA AAACAGGGAG | 540 |
| 20 | GGGGGATTC AGACTGTGAA GAAAGTTGAA TGGTGGTTTT TAAATTATAA AGTAATGTAT | 600 |
| | TAAAAGGTGC ATTAGGCTGT AGTTCTAATA TTGAGTTCAA CTGTGAAATC CATCAGATGT | 660 |
| | GCCAAATGGA GAAGACAGAA AGCAACAAAG TGAATTGTTT TTTAGCCCAA GTGGTACAGT | 720 |
| 25 | GAATTGCTT TAACAGATGT TGAAACTAA ATTTTCTACT GTATTCCCAG CACGGGTGAC | 780 |
| | TTCTTTTTCT CTTCAATAGC CAGAGATGAC TAATTTAAAT TTAGAACCAG ATTTTAATTT | 840 |
| 30 | AAATTAATAT TTCCATTAAT AACCTATTCA TTGCAGATAC CTATTATACT GTGTAACAGT | 900 |
| | TGTTTTGGAA ATTTTATGTA AAATTAAAC TATCAGTATT TTACAGATGT TTAAATTAGA | 960 |
| | CATGTTATTA ACAGGAACAG TGCAGAACT AGAATCAAGC CTTATAATAT CTTATAGACC | 1020 |
| 35 | ATGCATTTTG AAGTTAGTGT CCACTARGGT CCTATTAACT GTACATTGCA AGATTCATTA | 1080 |
| | TTTTGCCTCT GACACTAWGG GAAAATTTTT AGAAGCCAAT GGGACAGATT CCAGCCTTTA | 1140 |
| 40 | AGCACTGGGT ACTACAGCCG TAAAGGAAA TCCCGCCTGG TAGCCAGGGA TATNCCTCCC | 1200 |
| | CAGGTAAAN CCCCCAAAT NAA | 1223 |

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(2) INFORMATION FOR SEQ ID NO: 73:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1814 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

| | | |
|----|---|-----|
| | CAAGCTTTGT ACTTAGATCT TTTACTTAGA TCTGCTTTTT GTCTTATTCT TTTTAGTGA | 60 |
| 60 | TGTTTCCAAG GATTGTCTTC AGTCATGGCC TTGGGATTAA AGTGCTTCCG CATGGTCCAC | 120 |

| | | |
|----|--|------|
| | CCTACCTTTC GCAATTATCT TGCAGCCTCT ATCAGACCCG TTTCAGAAGT TACTACTGAAG | 180 |
| | ACAGTGCATG AAAGACAACA TGGCCATAGG CAATACATGG CCTATTTCAGC TGTACCAGTC | 240 |
| 5 | CGCCATTTTG CTACCAAGAA AGCCAAAGCC AAAGGGAAAG GACAGTCCCA AACCAGAGTG | 300 |
| | AATATTAATG CTGCCCTGGT TGAGGATATA ATCAACTTGG AAGAGGTGAA TGAAGAAATG | 360 |
| 10 | AAGTCTGTGA TAGAAGCTCT CAAGGATAAT TTCAATAAGA CTCTCAATAT AAGGACCTCA | 420 |
| | CCAGGATCCC TTGACAAGAT TGCTGTGGTA ACTGCTGACG GGAAGCTTGC TTAAACCAG | 480 |
| | ATTAGCCAGA TCTCCATGAA GTCGCCACAG CTGATTTTGG TGAATATGGC CAGCTTCCCA | 540 |
| 15 | GAGTGTACAG CTGCAGCTAT CAAGGCTATA AGAGAAAGTG GAATGAATCT GAACCCAGAA | 600 |
| | GTGGAAGGGA CGCTAATTCG GGTACCCATT CCCCAAGTAA CCAGAGAGCA CAGAGAAATG | 660 |
| 20 | CTGGTGAAAC TGGCCAAACA GAACACCAAC AAGGCCAAAG ACTCTTTACG GAAGGTTCGC | 720 |
| | ACCAACTCAA TGAACAAGCT GAAGAAATCC AAGGATACAG TCTCAGAGGA CACCATTAGG | 780 |
| | CTAATAGAGA AACAGATCAG CCAATGGCC GATGACACAG TGGCAGAACT GGACAGGCAT | 840 |
| 25 | CTGGCAGTGA AGACCAAAGA ACTCCTTGGA TGAAAGTCCA CTGGGGCCAG CAATACTCCA | 900 |
| | GAGCCCAGTT TCTGCTGGAT CCCATGGGTG GCACATTGGG ACTTCTCTCC CTCCTCCATC | 960 |
| 30 | TACACAGAAG ACTGTCACCA TGCTGACAGA AGCCTGTCCT TGTAAAGCCC AGCCTTCCAG | 1020 |
| | GGGAACACTC AGACATGTTT ATTCTCTTCC TGCTTCTGCT CTGGGCCGGT GGGTGGCTCT | 1080 |
| | CAGAAAWTAC TTGCTGCTGG CAAAAGGCCT GTACTCAGGC ATTTGCTTTG ACTTGATGTT | 1140 |
| 35 | GCCAAGGGAC TGAGGCCATT GGCAGGCTTA GTACCACCTG CTCCTCATCT TAGGAGTCTC | 1200 |
| | CTTTTCAAAT AATTAGGCTC TGTTCCTATT TTAAGACTCT GATATTGGCC TTCACCTGTG | 1260 |
| 40 | ACTGGACACT TTACTAGAGG CCCATTTTCA CTAAACAATA AAATCTAAAT AAATTGGAAG | 1320 |
| | GAATAACAAC CACAAAGGAA AGAATAGAGT TGGTCTGGAT TGATGATCAC TGAGGATCTG | 1380 |
| | TATGTGAGGC ACCCATAACA GTAGTTTTCG CTGTGAGTCG TCTTCACACA TGCTGTTTTT | 1440 |
| 45 | TCTGCCCTGGC TCTCTCTTCC CCTCCTTACC TGGCCAGTCC TGTTTATCAT CAGGCCCTGT | 1500 |
| | CTTGGATATC ACGTCTCTG GGAAGTCTTC TTTTCCCTC TAACCTAGGA CCCTCATTAC | 1560 |
| 50 | CGGCTCTCAT AGCACAGTCT ACTGCTTTGT ACGAATTCTA AGTATTCTTG TTGCACTTAA | 1620 |
| | TTAGCCTGTA TATCCTCAGA ACTTTGTGTA ATGCCTGGAG CATAGTAGGC AGTCATATGT | 1680 |
| | TGTATCGTGA ATAAATTGCA CATAGTAGCT ACCCAGCAAA TGCTGACTTC TTTTCTTTCT | 1740 |
| 55 | AGTCTTAACA CTCCTTTTCT AATNCATTTT CACTNMTGTA NTGTTCTCAA CATTACTTGG | 1800 |
| | TAGTGACAAA CTTT | 1814 |
| 60 | | |

(2) INFORMATION FOR SEQ ID NO: 74:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 4712 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

CATGGTACGC CTGCAGGTAC CGGTCCGGAA TTCCCGGGTC GACCCACGCG TCCGCCCAYG 60
CGTCCGGCGG CTCCGAGCCA GGGGCTATTG CAAAGCCAGG GTGCGCTACC GGACGGAGAG 120
15 GGGAGAGCCC TGAGCAGAGT GAGCAACATC GCAGCCAAGG CGGAGGCCGA AGAGGGGCGC 180
CAGGCACCAA TCTCCGCGTT GCCTCAGCCC CGGAGGCGCC CCAGAGCGCT TCTTGTCCTCA 240
20 GCAGAGCCAC TCTGCMTCG CCTGCCTCTC AGTGTMTCCA ACTTTGCGCT GGAAGAAAAA 300
CTTCCGCGCG GCGGCAGAA CTGCAGCGCC TCCTCTTAGT GACTCCGGGA GCTTCGGCTG 360
TAGCCKCGTM TGCGCGCCCT TCCAACGAAT AATAGAAATT GTTAATTTTA ACAATCCAGA 420
25 GCAGGCCAAC GAGGCTKTGC TCTCCCGACC CGAACTAAAG CTCCTCGCT CCGTGGCGTG 480
CTACGAGCGG TGTCTCTGG GGCTCCAATG CAGCGAGCTG TGCCCGAGGG GTTCGGAAGG 540
30 CGCAAGCTGG GCAGCGACAT GGGGAACGCG GAGCGGGCTC CGGGGTCTCG GAGCTTTGGG 600
CCCCTACCCA CGCTGCTGCT GCTCSCCGCG GCGCTACTGS CCGTGTGGA CCGACTCGGG 660
CGCCCCTCGG AGGAGGACGA GGAGCTAGTG GTGCCGAGC TGGAGCGCGC CCCGGGACAC 720
35 GGGACCACGC GCCTCCGCTT GCACGCTTTT GACCAGCAGC TGGATCTGGA GCTGCGGCCC 780
GACAGCAGCT TTTTGGCGCC CGGCTTCACG CTCCAGAACG TGGGGCGCAA ATCCGGGTCC 840
40 GAGAGCGCGC TTCCGGAAC CGACCTGGCG CACTGCTTCT ACTCCGGCAC CGTGAATGGC 900
GATCCACGCT CGGCTGCCGC CCTCAGCCTC TCGGAGGGCG TCGCGGCGC CTTCTACCTG 960
CTGGGGGAGG CGTATTTTCAT CCAGCCGCTG CCCGCCGCA GCGAGCGCCT CKCCACCGCC 1020
45 GCCCCAGGGG AGAAGCCGCC GGCACCACTA CAGTTCCACC TCCTGCGGCG GAATCGGCAG 1080
GGCGACGTAG GCGGCACGTG CGGGGTCTGT GACGACGAGC CCCGGCCGAC TGGGAAAGCG 1140
50 GAGACCGAAG ACGAGGACGA AGGACTGAG GCGGAGGACG AAGGGCCTCA GTGGTCCGCG 1200
CAGGACCCGG CACTGCAAGG CGTAGGACAG CCCACAGGAA CTGGAAGCAT AAGAAAGAAG 1260
CGATTTGTGT CCAGTCACCG CTATGTGGAA ACCATGCTTG TGGCAGACCA GTCGATGGCA 1320
55 GAATTCACAG GCAGTGGTCT AAAGCATTAC CTTCTCACGT TGTTTTCGGT GGCAGCCAGA 1380
TTGTWCAAAC ACCCCAGSAT TCGTAATTCA GTTAGCCTGG TGGTGGTGAA GATCTTGGTC 1440
60 ATCCACGATG AACAGAAGG GCCGGAAGTG ACCTCCAATG CTGCCCTCAC TCTGCGGAAC 1500

| | | |
|----|--|------|
| | TTTTGCAACT GGCAGAAGCA GCACAACCCA CCCAGTGACC GGGATGCAGA GCACTATGAC | 1560 |
| 5 | ACAGCAATTC TTTCACCAG ACAGGACTTG TGTGGGTCCC AGACATCTGA TACTCTTGGG | 1620 |
| | ATGGCTGATG TTGGAAGTGT GTGTGATCCG AGCAGAAGCT GCTCCCTCAT AGAAGATGAT | 1680 |
| | GGTTTACAAG CTGCCCTTCAC CACAGCCCAT GAATTAGGCC ACGTGTTTAA CATGCCACAT | 1740 |
| 10 | GATGATGCAA AGCAGTGTGC CAGCCTTAAT GGTGTGAACC AGGATTCCCA CATGATGGCG | 1800 |
| | TCAATGCTTT CCAACCTGGA CCACAGCCAG CCTTGGTCTC CTTGCAGTGC CTACATGATT | 1860 |
| 15 | ACATCATTTT TGGATAATGG TCATGGGGAA TGTGTGATGG ACAAGCCTCA GAATCCCAT | 1920 |
| | CAGCTCCAG GCGATCTCCC TGGCACCTCG TACGATGCCA ACCGGCAGTG CCAGTTTACA | 1980 |
| | TTTGGGGAGG ACTCCAAACA CTGCCCTGAT GCAGCCAGCA CATGTAGCAC CTTGTGGTGT | 2040 |
| 20 | ACCGGCACCT CTGGTGGGGT GCTGGTGTGT CAAACCAAAC ACTTCCCGTG GCGGATGGC | 2100 |
| | ACCAGCTGTG GAGAAGGGAA ATGGTGTATC AACGGCAAGT GTGTGMACAA AACCGACAGA | 2160 |
| 25 | AAGCATTTTG ATACGCCTTT TCATGGAAGC TGGGGAATGT GGGGGCCTTG GGGAGACTGT | 2220 |
| | TCGAGAACGT GCGGTGGAGG AGTCCAGTAC ACGATGAGGG AATGTGACAA CCCAGTCCA | 2280 |
| | AAGAATGGAG GGAAGTACTG TGAAGGCAAA CGAGTGCCT ACAGATCCTG TAACCTTGAG | 2340 |
| 30 | GACTGTCCAG ACAATAATGG AAAAACCTTT AGAGAGGAAC AATGTGAAGC ACACAACGAG | 2400 |
| | TTTTCAAAAG CTTCCTTTGG GAGTGGCCT GCGGTGGAAT GGATTCCCAA GTACGCTGGC | 2460 |
| 35 | GTCTCACCAA AGGACAGTG CAAGCTCATC TGCCAAGCCA AAGGCATTGG CTACTTCTTC | 2520 |
| | GTTTTGCAGC CCAAGGTGT AGATGGTACT CCATGTAGCC CAGATTCCAC CTCGTCTGT | 2580 |
| | GTGCAAGGAC AGTGTGTAAA AGCTGGTGT GATCGCATCA TAGACTCCAA AAAGAAGTTT | 2640 |
| 40 | GATAAATGTG GTGTTTGGG GGGAAATGGA TCTACTTGTA AAAAAATATC AGGATCAGTT | 2700 |
| | ACTAGTCAA AACCTGGATA TCATGATATC ATCACAATTC CAACTGGAGC CACCAACATC | 2760 |
| 45 | GAAGTGAAAC AGCGGAACCA GAGGGATCC AGGAACAATG GCAGCTTTCT TGCCATCAAA | 2820 |
| | GCTGCTGATG GCACATATAT TCTTAATGGT GACTACACTT TGTCCACCTT AGAGCAAGAC | 2880 |
| | ATTATGTACA AAGGTGTGT CTTGAGGTAC AGCGGCTCCT CTGCGGCATT GGAAAGAATT | 2940 |
| 50 | CGCAGCTTTA GCCCTCTCAA AGAGCCCTTG ACCATCCAGG TTCTTACTGT GGGCAATGCC | 3000 |
| | CTTCGACCTA AAATTAAATA CACCTACTTC GTAAAGAAGA AGAAGGAATC TTTCAATGCT | 3060 |
| 55 | ATCCCCACTT TTTGAGCATG GGTCAATTGAA GAGTGGGGCG AATGTTCTAA GTCATGTGAA | 3120 |
| | TTGGGTGGC AGAGAAGACT GGTAGAATGC CGAGACATTA ATGGACAGCC TGCTTCCGAG | 3180 |
| | TGTGCAAAGG AAGTGAAGCC AGCCAGCACC AGACCTTGTG CAGACCATCC CTGCCCCCAG | 3240 |
| 60 | TGGCAGCTGG GGGAGTGGTC ATCATGTTCT AAGACCTGTG GGAAGGGTTA CAAAAAAGA | 3300 |

| | | |
|----|--|------|
| | AGCTTGAAGT GTCTGTCCCA TGATGGAGGG GTGTTATCTC ATGAGAGCTG TGATCCTTTA | 3360 |
| | AAGAAACCTA AACATTTTCAT AGACTTTTGC ACAATGGCAG AATGCAGTTA AGTGGTTTAA | 3420 |
| 5 | GTGGTGTTAG CTTTGAGGGC AAGGCAAAGT GAGGAAGGGC TGGTGCAGGG AAAGCAAGAA | 3480 |
| | GGCTGGAGGG ATCCAGCGTA TCTTGCCAGT AACCAGTGAG GTGTATCAGT AAGGTGGGAT | 3540 |
| 10 | TATGGGGGTA GATAGAAAAG GAGTTGAATC ATCAGAGTAA ACTGCCAGTT GCAAATTTGA | 3600 |
| | TAGGATAGTT AGTGAGGATT ATTAACCTCT GAGCAGTGAT ATAGCATAAT AAAGCCCCGG | 3660 |
| | GCATTATTAT TATTATTTCCT TTTGTTACAT CTATTACAAG TTTAGAAAAA ACAAAGCAAT | 3720 |
| 15 | TGTCAAAAAA AGTTAGAACT ATTACAACCC CTGTTTCCTG GTACTTATCA AATACTTAGT | 3780 |
| | ATCATGGGGG TTGGGAAATG AAAAGTAGGA GAAAAGTGAG ATTTTACTAA GACCTGTTTT | 3840 |
| 20 | ACTTTACCTC ACTAACAATG GGGGGAGAAA GGAGTACAAA TAGGATCTTT GACCAGCACT | 3900 |
| | GTTTATGGCT GCTATGGTTT CAGAGAATGT TTATACATTA TTTCTACCGA GAATTAAAAC | 3960 |
| | TTCAGATTGT TCAACATGAG AGAAAGGCTC AGCAACGTGA AATAACGCAA ATGGCTTCCT | 4020 |
| 25 | CTTTCCTTTT TTGGACCATC TCAGTCTTTA TTTGTGTAAT TCATTTTGAG GAAAAACAA | 4080 |
| | CTCCATGTAT TTATTCAAGT GCATTAAAGT CTACAATGGA AAAAAAGCAG TGAAGCATT | 4140 |
| 30 | GATGCTGGTA AAAGCTAGAG GAGACACAAT GAGCTTAGTA CCTCCAACCT CCTTTCTTTC | 4200 |
| | CTACCATGTA ACCCTGCTTT GGAATATGG ATGTAAAGAA GTAACCTGTG TCTCATGAAA | 4260 |
| | ATCAGTACAA TCACACAAGG AGGATGAAAC GCCGGAACAA AAATGAGGTG TGTAGAACAG | 4320 |
| 35 | GGTCCACAG GTTTGGGGAC ATTGAGATCA CTTGTCTGTG GGTGGGGAGG CTGCTGAGGG | 4380 |
| | GTAGCAGGTC CATCTCCAGC AGCTGGTCCA ACAGTCGTAT CCTGGTGAAT GTCTGTTTCA | 4440 |
| 40 | CTCTCTGTG AGAATATGAT TTTTCCATA TGTATATAGT AAAATATGTT ACTATAAATT | 4500 |
| | ACATGTACTT TATAAGTATT GGTTGGGTG TTCCTTCCAA GAAGGACTAT AGTTAGTAAT | 4560 |
| | AAATGCCTAT AATAACATAT TTATTTTAT ACATTTATTT CTAATGAAAA AAACTTTAA | 4620 |
| 45 | ATTATATCGC TTTTGTGGAA GTGCATATAA AATAGAGTAT TTATACAATA TATGTTACTA | 4680 |
| | GAAATAAAAG AACACTTTTG GAAAAA AAAA | 4712 |
| 50 | | |

(2) INFORMATION FOR SEQ ID NO: 75:

- 55 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1885 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- 60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

| | | |
|----|--|------|
| | ATGCCARGAA GACTGATGGA GCAGGCTTGC AATAATTAAAG TNCCAACCAA GAAGCTGAAG | 60 |
| 5 | AAATWTGAGA AAGAATATCC AGACAATGCG AGAGAGTCAG CTGCAACAGG AAGACCCAAT | 120 |
| | GGATAGATAC AAGTTTGTAT ATTTGTAGGT AACTCCAGCT GTTGCAITTA TACTGGGAAT | 180 |
| 10 | CTTCATAAGA AGCTGAGAGA AAGAGAGGGG AAAAAGAAAG TGGCTTTCTA CTTCAAAAA | 240 |
| | TGAAACAAAA AGGAAAAATG GCAAAGTACT GTTTTAGCTG TGCATGTCAT ATCCACAAAG | 300 |
| | ACTTTTAGCA GGTGAAGTGT TCCAAGACTG ACACAAGGAT GTTTCAAACT TGCCTCTGTC | 360 |
| 15 | TGTAGAAAAT GTTAAAAATA CCAACTCACT TGGAAGGAAA AATAAAAATC ACAAAGGTAT | 420 |
| | ATTGAGCACA GTAGTGGTGT TTGTGCAAC ATTTATTTCC ACAAATGAAT TTATGAACAA | 480 |
| 20 | CAGTGATATT TGAAGTAAAG TATGAAGTTT CAGAATCAAA ATAATTTTCAT TTTAATACGT | 540 |
| | TCNGTTAATT GTGAATCTCT TCMATGGTAA TTAGCAACAC TGTTCACAGG ATGCAAGTT | 600 |
| | GGGAAACACT TATTTCCAAC TTATTTTTTT CCAAGTAAAA TATTATCTCT CTTCACATG | 660 |
| 25 | CTTTAACTTT TCAGACTCAC ACAGATACGT WACAGCTCCC TTCTCCCTCC ATATCAATAC | 720 |
| | ACTAAGATAA AAGAATACTG TATTTTCAGC ACTGAGCAGC AGTGCCAAAA TCTCTGCCA | 780 |
| 30 | AGAAATGGAC TGTGTGGCAT TATTAATTAA ATCACCACCA TTGGGATGAC TTCCACTTTT | 840 |
| | GTAAGTAGAG TTATCTTTAT GTGGTCAGAG CTGGACATAG GCAGCATAGT CACACAGAAC | 900 |
| | ATCTTATCTC TGTGCKGAA TKGAATAGCA TGGGATGTGT GCAGAGGAAC ATGGKGGGAG | 960 |
| 35 | TATGTAGGTT TKGTAGTCAG ACAGACCKGA ACTCAAATCT TGYTCATTTT TTAGAGCACA | 1020 |
| | GGATTTGGAY TCCAAATTGA GGGTTTAAAT CCCCATGCCA CCATTTCAGCA TCTTCGACTA | 1080 |
| 40 | GTTATTGAAC CTYTTCTCA TSKATAAAAG ATATAGTGTT TCTGATTCTT TGATGGATTG | 1140 |
| | TTACAAGGAT GAGGGATGCT GTATGTTAAG GACTCAGCTC ATAGTTGIGT TCAATAAATG | 1200 |
| | GCTGTTATTT TATGAAGCCT ACTACTACAG ATTATGCAAT TATTACTAGA ATAATGCCAC | 1260 |
| 45 | CTTATGTGGG TCTTCCCCTC TAGTCCCTTA TTGATTGTTT TTATTTCTCT CAAGTATTGC | 1320 |
| | CAACCAATAA TCTCCCCTTG CTTATAGAAG TGGTTCAAGA TCTGATTATA AAATCCCACA | 1380 |
| 50 | TACTTCTATA GCAGATAACT ATTAACAGAT AATGTTTGRA CTAATTTTAC CACCAACATT | 1440 |
| | CCCCCTCAAT AAAACAGCT TTTAATGTAA ATCACATAGC ATACTGCTTT AGAAAGGCTT | 1500 |
| | GAAGGTAGTA ATTATAAAT ATTATTAAGC ATCCAAAATG AAGGTCTCCT TTTGCTAATA | 1560 |
| 55 | TCATTCAGAT TTTCTTATTA CTACAATTAT TATGAATAAA TTCTGTGAAG AGTGCTTTAA | 1620 |
| | AATAAGAGAG AAATGGRAGA CCAAACCTGT ACATTTAAAA TCAGGCTGGA ATTGAACTTG | 1680 |
| 60 | TTATGTGTC TTAATCCTT TTTGTGCCA AAGCAGGTAT GTATACATTA ATAGTAAGAT | 1740 |

GTACATTATT TTAAAGTAC TTATMACATG TAAGATTATC AATATGTATA GTTTTATTG 1800
AGAGATCAAA GTAGGATTAA ACTTCTTGTT TTGAAAGCAG GCATTACTTT TTAAAAAAA 1860
5 AAAAAAAAAA AAAAAAAAAA AAAAA 1885

10 (2) INFORMATION FOR SEQ ID NO: 76:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 890 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:

20 TTCAAACTAG CAAAAATGT ATGAACTAT GAAGCTCGAT GCGTGTRATC ATCAGCAGAG 60
GCCGACGCTG CAGGCAGGGC CAAAGCTTCT GACCTTGGCC CCCAGGGAGG AACCCAGAGG 120
CCAGTCAGGG AGGGGACGCG AGCTCAGCGC CAGGCAGCGC CACAGCACTG GCGACCCTCA 180
25 GGGAGAACAG GCACTACCCA GGGCTGGATG CGTAACGGGC CCCCCGGCCA CACCCACCG 240
CCCATCAGAG CCGCAGCTCC TGAGAACGCA TCCGGATGCN AGGCCAAAGT CAGCCATGGC 300
30 ACAAACTTT GTGCATCAAG GTCTGTGTC TCTGCAACAA CTCACCACAA ACAGAAGGGT 360
GGAAACCTCC ATGTCATCGG ACGGCCACGG SCAGAATCCA ACGCCATCTC CCTGGGCTGA 420
TGTCGTGCA AGCAGGGCTG ATGCCGTAGC TTTCCTGGCT TCTGGAARCT GCCACAGCCC 480
35 CTGGCTCATG GSACCATCCT CACATCCTCT GAATCCACAT TCTCTCTGA ATCTCCCGCC 540
TCCCTCTTTC CACTGTAAGG ACCCTGTGAT GACACTGCAC CCTCAGACCC TGGTAACCCA 600
40 GGGTCATCTT TCCACCTCAG GCGCTCTGAC TTAAGCCTGC CTGGAGGGTC CCTGTGGTCA 660
CATTCATGGG TTCCAGGCTT CAGACACGGC CACTTTGTGG GATCATTACT CTGCCTACCA 720
CACCATGTGG CCCTGTGTGT GTTTTCAGGG GGCATTGTCG CYTATATGCA AATAATACAT 780
45 ATATGAATAA ACGTGTGAAT GGTGGTCACG TAGGAGARGG CATCTGTATG GGGCCACACC 840
TGTAATAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 890

50

(2) INFORMATION FOR SEQ ID NO: 77:

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1657 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
60 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

| | | |
|----|--|------|
| | AGAAAC ECCT TCCCCACATC TTCCAGCACC TGCGCGCCTG AATCCGTCCC ACCCAGGCCC | 60 |
| 5 | AGACGCAGGC TTCTTCTCGG GTCTTGGTCC TGCATCCTCT CTCTCCAGA GCCTCCGTTA | 120 |
| | GGGGTGGGAA AGGACTTTGC CATAGGTGCG TGAGGCCACC ATCTGCTCTC TTAGTGGCCA | 180 |
| 10 | AGGGCGTAAA AAGATAGTCY TCCCATTAGC TAGAGAGCAA ACCCCAGAAA GCCTATTGGC | 240 |
| | TGCGCCGTCC GCGGGCCTTG GTCCGNTTTG AAGGCGGGCT GCGGCTGCGA GAGGAGGGCG | 300 |
| | GGCGGGAGGC TAGCTGTGTG CTGTGGTTGCT CGGAGGCACG TGTGCAGTCC CGGAAGCGGC | 360 |
| 15 | GAGGGGAAAC TGCTCCGCGC GCGCCGCGGG AGGAGGAACC GCCCGTCTCT TTAGGGTCCG | 420 |
| | GGCCCGGCGG GGCATGGATT CAATGCCTGA GCCCGCGTCC CGCTGTCTTC TGCTTCTTCC | 480 |
| 20 | CTTGCTGCTG CTGCTGCTGC TGCTGCTGCC GGCCCCGAG CTGGGCCGA GCCAGGCCGG | 540 |
| | AGCTGAGGAG AACGACTGGG TTCGCCTGCC CAGCAAATGC GAAGGGACTT GCGGTTAATC | 600 |
| | GAAGTCACTG AGAACCATT TCAAGAGGCT CCTGGATTAT AGCCTGCACA AGGAGAGGAC | 660 |
| 25 | CGGCAGCAAT CGATTTGCCA AGGGCATGTC AGAGACCTTT GAGACATTAC ACAACCTGGT | 720 |
| | ACACAAAGGG GTCAAGGTGG TGATGGACAT CCCCTATGAG CTGTGGAACG AGACTTCTGC | 780 |
| 30 | AGAGGTGGCT GACCTCAAGA AGCAGTGTGA TGTGCTGGTG GAAGAGTTTG AGGAGGTGAT | 840 |
| | CGAGGACTGG TACAGRAACC ACCAGGAGGA AGACCTGACT GAATTCTCTT GCGCCAACCA | 900 |
| | CGTGCTGAAG GGAAAAGACA CCAGTTGCCT GGCAGAGCAG TGGTCCGGCA AGAAGGGAGA | 960 |
| 35 | CACAGCTGCC CTGGGAGGGA AGAAGTCCAA GAAGAAGAGC AKCAGGGCCA AGGCAGCAGG | 1020 |
| | CGGCAGGAGT AGCAGCAGCA AACAAAGGAA GGAGCTGGGT GGCCTTGAGG GAGACCCAG | 1080 |
| 40 | CCCCGAGGAG GATGAGGGCA TCCAGAAGGC ATCCCCTCTC ACACACAGCC CCCCTGATGA | 1140 |
| | GCTCTGAGCC CACCCAGCAT CCTCTGTCTT GAGACCCCTG ATTTTGAAGC TGAGGAGTCA | 1200 |
| | GGGGCATGGC TCTGGCAGGC CGGGATGGCC CCGCAGCCTT CAGCCCCCTC TTGCCTTGGC | 1260 |
| 45 | TGTGCCCTCT TCTGCCAAGG AAAGACACAA GCCCCAGGAA GAACTCAGAG CCGTCATGGG | 1320 |
| | TAGCCACGC CGTCCCTTCC CTTCCCAAG TGTCTCTCTC CTGACCCAGG GTTCAGGCAG | 1380 |
| 50 | GCCTTGTTGGT TTCAGGACTG CAAGGACTCC AGTGTGAACT CAGGAGGGGC AGGTGTCAGA | 1440 |
| | ACTGGGCACC AGGACTGGAG CCCCCCTCGG AGACCAAAT CACCATCCCT CAGTCTCTCC | 1500 |
| | CAACAGGGTA CTAGGACTGC AGCCCCCTGT AGCTCCTCTC TGCTTACCCC TCCTGTGGAC | 1560 |
| 55 | ACCTTGCACT CTGCCTGGCC CTTCCCAGAG CCCAAAGAGT AAAAATGTTT TGGTTCTGAW | 1620 |
| | RAAAAAAAAA AAAAAAAAAA CCCCCGGGGG GGCCCGT | 1657 |

(2) INFORMATION FOR SEQ ID NO: 78:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 2015 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

| | | |
|----|--|------|
| | GGCCGGGCTG AGAGAAGAGC TTGCGGGGTT TGCGGTTGAT GGCCCCGACT GAAGGGCTGG | 60 |
| | AGGCGGTGTA TGCCGCTGTT CTGCTGTG CTCCCGACAC CTCGTCGCG TTCTGGTCAT | 120 |
| 15 | GAGAGGAGAC AGAGGCCTGA AGCAAAGACA TCTGGGTCAG AGAAAAAGTA TTAAAGGGCC | 180 |
| | ATGCAAGCCA ATCGTAGCCA ACTGCACAGT CCTCCAGGAA CTGGAAGCAG TGAGGATGCC | 240 |
| 20 | TCAACCCCTC AGTGTGTCCA CACAAGATTG ACAGGAGAGG GTTCTTGCCC TCATTCTGGA | 300 |
| | GATGTTTATA TCCAGATAAA CTCCATACCT AAAGAATGTG CAGAAAAATGC AAGCTCCAGA | 360 |
| | AATATAAGGT CAGGTGTCCA TAGCTGTGCC CATGGATGTG TACACAGTCG CTTACGGGGT | 420 |
| 25 | CACTCCCACA GTGAAGCAAG GCTGACTGAT GATACTGCCG CAGAATCTGG AGATCATGGT | 480 |
| | AGTAGCTCCT TCTCAGAATT CCGCTATCTC TTCAAGTGGC TGCAAAAAAG TCTTCCATAT | 540 |
| 30 | ATTTTGATTC TGAGCGTCAA ACTTGTATG CAGCATATAA CAGGAATTC TCTTGGAATT | 600 |
| | GGGCTGCTAA CAACTTTTAT GTATGCAAAC AAAAGCATTG TAAATCAGGT TTTTCTAAGA | 660 |
| | GAAAGGTCTT CAAAGATTCA GTGTGCTTGG TTAGTGTAT TCTTAGCAGG ATCTTCTGTT | 720 |
| 35 | CTTTTATATT ACACCTTTCA TTCTCAGTCA CTTTATTACA GCTTAATTTT TTAAATCCT | 780 |
| | ACTTTGGACC ATTTGAGCTT CTGGGAAGTA TTTKGGATTG TTGGAATNAC AGACTTCATT | 840 |
| 40 | CTGAATTTCT TTTTCATGGG CTTAAATGC CTTATTTTAT TGGTGCCTTC TTTTCATCATG | 900 |
| | CCTTTTAAAT CTAAGGGTTA CTGGTATATG CTTTATAGAAG AATTGTGTCA ATACTACCGA | 960 |
| | ACTTTTGTTC CCATACCACT TTGGTTTCGC TACCTTATAA GCTATGGGGA RTTTGGTMAC | 1020 |
| 45 | GTAAC TAGAT GGATCTTGG GATACTGCTG GCTTTACTCT ACCTCATATT AAAACTTTTG | 1080 |
| | GAATTTTITG GGCATCTGAG AACTTTCAGA CAGGTTTAC GAATATTTT TACACMACCM | 1140 |
| 50 | AGTTATGGAG TGGCTGCCAG CAAGAGACAG TGTTCAGATG TGGATGATAT TTGTTCAATA | 1200 |
| | TGTCAAGCTG AATTTCAGAA GCCAATCTCT CTCATTTGTC AGCATATATT TTGTGAAGAG | 1260 |
| | TGCATGACCT TATGGTTTAA CAGAGAGAAA ACATGTCCAC TCTGCAGAAC TGTGATTTCA | 1320 |
| 55 | GACCATATAA ACAAATGGAA GGATGGAGCC ACTTCATCAC ACCTTCAAAT ATATTAAGTT | 1380 |
| | GTATAAACTA TCAAGCCAC AAAATACTAA TGTCATTTGG TCATAATGAC TACTGATAAG | 1440 |
| 60 | GCATCAGAAT GGATTTTCAG GGCTACCAGA AAAATGTTTC CAGATGGTTT TAGAATGTAG | 1500 |

5 GACTTATGAT CCAATTCACC AAAAGATTA ATGAAACCAC CCTGTGTTTT AAAATATATA 1560
 TAATGTTCAA CCTAATGTAT ATGCAACATT TATTCTATTC TAATTATTTG ACAGGTAAC 1620
 GCAGTGTTAA ATTGTAAATG TGTTCCTTTT ATGTTACCAA AACAGCAATT TGAAATTAGA 1680
 ACTAGTGGTT TTAGAGAACT CAGGTATTCT TTCTGACAT TGTTCCTAGA ATAAAGAATA 1740
 10 TTTTCATAA TATTTAAGA TACATACTAT CTAAAAGTAG AATTTGTTC AGCATTGACT 1800
 TTTATAATTC CCATCCTAAA AATCTTAAT ATTTTCATAA AATTTGTATT TTTAAATGAA 1860
 AATTCTAAAT GTTGTATTTT ATCAGTAACA TTTTCTAAGT GAAGATTAAT TTAGTGAGGA 1920
 15 TGATACATTA TAGTATTGTA TTATCTCTG TAGTAAGATT AGTAATAAGT GAAAATAAAT 1980
 GATTTAAATT CAAAAAATAA AAAAAANTNA CTCGA 2015

20

(2) INFORMATION FOR SEQ ID NO: 79:

25

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1213 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

AGCCTAGTTA CAGATTGCAC TCGTCAGAC TGTTCACAC CCAGAAGACG TCAGGTGACT 60
 35 TCAGTCTGTC TGCAGTTGTG CAGCAGAGGA GACTGCAGAC TTCGGTTGAG GAAACGGGTG 120
 TTTTCATGCT CAGGGAGTAG GTTGTGTCAG TTACAGCTTT TCTGTTGTA TGCATAATTA 180
 40 ATAATTGGAG CTGCAAASCA GATCGTGACA AGAGATGGAC GGTGAGAAGA AAAATTGGAA 240
 GGACAAGGTT GTTGACCTCC TGTACTGGAG AGACATTAAG AAGACTGGAG TGGTGTGTTG 300
 TGCCAGCCTA TTCCTGCTGC TTTCATTGAC AGTATTCAGC ATTGTGAGCG TAACAGCCTA 360
 45 CATTGCCTTG GCCCTGCTCT CTGTGACCAT CAGCTTTAGG ATATACAAGG GTGTGATCCA 420
 AGCTATCCAG AAATCAGATG AAGGCCACCC ATTCAGGGCA TATCTGGAAT CTGAAGTTGC 480
 TATATCTGAG GAGTTGGTTC AGAAGTACAG TAATCTGCT CTGGTCATG TGAAGTGCAC 540
 50 GATAAAGGAA CTCAGGCGCC TCTTCTTAGT TGATGATTA GTTGATTCTC TGAAGTTTGC 600
 AGTGTGATG TGGGTATTTA CCTATGTTG TGCCTTGTTT AATGGTCTGA CACTACTGAT 660
 55 TTGGCTCTC ATTTCACTCT TCAGTGTTC TGTATTAT GAACGGCATC AGGCACAGAT 720
 AGATCATTAT CTAGGACTTG CAAATAAGAA TGTAAAGAT GCTATGGCTA AAATCCAAGC 780
 60 AAAAAATCCCT GGATTGAAGC GCAAAGCTGA ATGAAAACGC CAAAAATAAT TAGTAGGAGT 840

TCATCTTTAA AGGGGATATT CATTGATTA TACGGGGGAG GGTACGGGAA GAACGAACCT 900
 TGACGTTGCA GTGCAGTTTC ACAGATCGTT GTTAGATCTT TATTTTTAGC CATGCACTGT 960
 5 TGTGAGGAAA AATTACCTGT CTGACTGCC ATGTGTTTAT CATCTTAAGT ATTGTAAGCT 1020
 GCTATGTATG GATTTAAACC GTAATCATAT CTTTTTCCTA TCTGAGGCAC TGGTGAATA 1080
 10 AAAAACCTGT ATATTTTACT TTGTTGCAGA TAGTCTTGCC GCATCTTGCC AAGTTGCAGA 1140
 GATGGTGGAG CTAGAAAAAA AAAAAAAAAA ANCTYGAGAC TAGCGGCACG AGGGGGGGCC 1200
 CGTACCCAAN ACG 1213

15

(2) INFORMATION FOR SEQ ID NO: 80:

20

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1391 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

GCAGAGGCCG ACTGCTGAAG GTGGTTTGGC TCGACATGGC GGTACCCCTG AGTCTCTTGC 60
 30 TGGCGCGGCG CGTTTGGCGG CGTCACTCG CTGTGGGTTT GCGACCCGGG GGGTGGCGGG 120
 CCCAGGCCCT ATTGGCCGGG AGCCGGACCC CGATTCCGAC TGGGAGCCGG AGGAACGGGA 180
 35 GCTGCAGGAG GTGGAGAGCA CCTGAAACG ACAGAAACAA GCAATCCGAT TCCAGAAAAT 240
 TCGGAGGCAA ATGGAGGCGC CTGGTGCCCC GCCCAGGACC CTGACGTGGG AAGCCATGGA 300
 GCAGATACGG TATTTACATG AGGAATTTCC AGAGTCCTGG TCAGTTCCCA GGTGGCTGA 360
 40 AGGCTTTGAT GTCAGCACTG ATGTGATCCG AAGAGTTTAA AAAAGCAAGT TTTTACCCAC 420
 ATTGGAGCAG AAGCTGAAGC AGGATCAAAA AGTCCTTAAG AAAGCTGGGC TTGCCCACTC 480
 45 GCTGCAGCAC CTCCGGGGCT CTGAAATAC CTCAAAGCTG CTCCCTGCAG GCCACTCTGT 540
 ATCAGGCTCT TTGCTTATGC CAGGGCATGA AGCCTCATCT AAAGACCCAA ATCAGAGCAC 600
 AGCTTTGAAA GTGATAGAGT CAGACACTCA CAGGACAAAT ACACCAAGGA GAAGGAAGGG 660
 50 AAGAAATAAA GAAATCCAGG ACCTGGAGGA GAGCTTTGTG CCTGTTGCTG CACCCCTAGG 720
 TCATCCAAGA GAGCTGCAGA AGTACTCCAG TGATTCTGAG AGCCCCAGAG GAACTGGCAG 780
 TGGTGCCTTG CCAAGTGGTC AGAAGCTGGA GGAGTTGAAG GCAGAGGAGC CAGATAACTT 840
 55 CAGCAGCAAA GTAGTGCAGA GGGGCCGAGA GTTCTTTGAC AGCAACGGGA ACTTCCTGTA 900
 CAGAATTTGA GTCGGGGCTT GGCTTATGGA GATGCCTCGT GAAACACAGC TGGGCAAGTA 960
 60 TTAATGTATA TGAACAGCC TGGATTCTCT CATATGGATA AGCCACCTTG GAATAGGAAG 1020

5 AGGTGTTGAG CCTGGACTGT GGGAGGAAAG AGCTGCGTGG ATAGATTCAA ACTTCCTGTG 1080
 GTAGTGCTCC CAGTCTGACC TCTGTAGACC TTCAGTACTC ACTCTTCTTG CTTAGGCTCT 1140
 CTGTGTGTG AAAGCCATCC CGTGTTCAT GTGTGTAC AATTTCTGT GATACTTGCA 1200
 ATTTATGTTT GAGAAGAAGT GAAAAGTTTG CCTTCTGACC TCATTTCTT CTTGATCAGT 1260
 10 GAACACTAAC ATTTTGGGGA CAACCTAGTC AATTGGTTTT CTTTACAACA AAATAAAGTA 1320
 AAATGTAGCA AAAAAAAAAA AAAAAAACN CGGGGGGGGC CCGTCCCAT GCCCCAAAGG 1380
 GGGCCGAATA A 1391
 15

(2) INFORMATION FOR SEQ ID NO: 81:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1008 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

20 TGACATCGCC CTCATGAAGC TGCAGTTCCT ACTCACTTTC TCAGGCACAG TCAGGCCCAT 60
 30 CTGTCTGCCC TTCTTTGATG AGGAGCTCAC TCCAGCCACC CCACTCTGGA TCATTGGATG 120
 GGGCTTTACG AAGCAGAATG GAGGAAGAT GTCTGACATA CTGCTGCAGG CGTCAGTCCA 180
 35 GGTCAATGAC AGCACACGGT GMAATGCAGA CGATGCGTAC CAGGGGGAAG TCACCGAGAA 240
 GATGATGTGT GCAGGCATCC CGGAAGGGGG TGTGGACACC TGCCAGGGTG ACAGTGGTGG 300
 GCCCCTGATG TACCAATCTG ACCAGTGGCA TGTGGTGGGC ATCGTTAGCT GGGGCTATGG 360
 40 CTGCGGGGGC CCGAGCACCC CAGGAGTATA CACCAAGGTC TCAGCCTATC TCAACTGGAT 420
 CTACAAATGTC TGAAGGCTG AGCTGTAATG CTGCTGCCCC TTTGCAGTGC TGGGAGCCGC 480
 45 TTCTTCTCTG CCTGCCCCAC CTGGGGATYC CCCAAAGTCA GACACAGAGC AAGAGTCCCC 540
 TTGGGTACAM CCTYTGCCC ACAGCCTCAG CATTTCTTGG AGCAGCAAAG GGCCTCAATT 600
 CCTATAAGAG ACCCTCGCAG CCCAGAGGCG CCCAGAGGAA GTCAGCAGCC CTAGCTCGGC 660
 50 CACACTTGGT GCTCCAGCA TCCAGGGAG AGACACAGCC CACTGAACAA GGTCTCAGGG 720
 GTATTGCTAA GCCAAGAAGG AACTTTCCCA CACTACTGAA TGGAAGCAGG CTGTCTTGTA 780
 55 AAAGCCCAGA TCACTGTGGG CTGGAGAGGA GAAGGAAAGG GTCTGCGCCA GCCCTGTCCG 840
 TCTTACCCA TCCCCAAGCC TACTAGAGCA AGAAACCACT TGTAATATAA AATGCACTGC 900
 CCTACTGTG GTATGACTAC CGTTACCTAC TGTGTTCATT GTTATTACAG CTATGGCCAC 960
 60

TATTATTAAA GAGCTGTGTA ACATCAAAAA AAAAAAAAAA AAACTCGA

1008

5

(2) INFORMATION FOR SEQ ID NO: 82:

(i) SEQUENCE CHARACTERISTICS:

10

- (A) LENGTH: 1261 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

15

GTTTTCAAAC TCATTCTTAA GCCAAATAGT TTAGATAAAT ATTTACCCCTT ATATTGCGG 60

GGAATTCAGG CTCACCATTT GCCGAGGCAA GCCCATCAAC AGTCTAGAGG CATATTCTGT 120

20

GTCATTCCCT CCCGCTCCT TCATAGAATA CTACTTTTTC CTTTGTCTC CTGGCCATTC 180

TCCATCATCT GCTGATTATT GCTAACCACA GGATGCTGGC AAAGCTTACA GTGATAGGCA 240

25

CATGTGTTCA GTGATGTCCA ATACACTCTT ATCAGTGG TTATTGCTTC TTAATCTTTT 300

CAAATGCATT ATTCTACCCC TCAACCTAYA TCCAATCATT AGAACTATAC CTGACTGGAG 360

CCCAGAACTT GGGACCAATA CTTAATTCAA ATAGCAGGGG CTGCTCACA AACATTAAGC 420

30

CCAAMAAGAA GCACAGCACT TTKGAAAAGT CAAATAGGSC TTTGGTAGCT CTGTACATT 480

NGCAATTTAC ATTGTTATTA AGTTTATAGC ACTAATAACA CTTAGTCGT GAATCTACAG 540

35

TCTCAATATG ATAAGTCTTA GAACATGTTT TAGAAATAGT GGTACCTTGC TGCTATTATA 600

CTTAGTAACT TATACCCCAA TATAATAATA AGTATTAAAT ACAGATTGTG TATGCATTCT 660

TTGTGTGTAT ATGCCAACTG TACTACTTAA CCTCACTGAT GAGCAATTAG AAAAAATACAC 720

40

AAATGTGCAT AGTGAAAATA AGTCTTGGTC AATTCAGATG ATACGTGAAC CTGATAAATG 780

CTCTAATAGA TATGCTATTT TGCTCTGTAT TGCTTGTTTT ACAGTATGGT GCATGTTGTT 840

45

TGCTAAGTAA AATGATAATA ATAATAAAGT ATACCCAATT TTAAGGTTAG AATTAAATTT 900

TTGCACATAT GCTTCTTGAT ATTCTGAAAT GTATTCTGTG GSTTMAATTAT CTTATTCTA 960

CACATTKMGC TWGGCTTTTT ACCCCTAGGA AATAACTGTC CAAGTATATA TCTCGTCTTC 1020

50

TTTCTTGTA CTTTGATTAA ACTGCTTACT TCAACTTACA ACATTGTAAA GCCAGAATAC 1080

CTCATTTTAA CAGTGAAAAA AAATATTATG ACCTGATGTG TTCTCTTGTA TTTGATTGA 1140

55

ACTACCTAAA TAGGCTTAAC TGTAATAATA AATATACAAT TTTGGCAAAA AAAAAAAAAA 1200

AAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAGGGCGGC 1260

C

1261

60

(2) INFORMATION FOR SEQ ID NO: 83:

- 5 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1045 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
10 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

TCGAGTMTT TTTTMTTMTT TTTTAAGCAA CAGTTTATTG AGACGGAAAA AATATGATCC 60
15 AGCAAAGGCG AGGAGGCGAG CCGGGCCCCG AGCCAGCTGG TGTCATTGTC ACTGGCTCCC 120
AAACCTGACT CCTGTGGACG TGTCTGTACC CCAAACACAG CTGCCCCACC CAGCCCTGGC 180
ACAGAGCCCT TCTGAAAGAA AGAAAAAGA AGAAAGACGC GGCACCTGAC GCCAGCGGGT 240
20 AAAAGCAGGG CCCAGAGGC ATTTATTGAA AACACAGCAT CAAAACACG ACATCTAGGC 300
CAGGCGCGAT GGTACAGTG ATGAGAGGGT CACTAGACAA TTATCCACAA TTCTACGACA 360
25 TGAGACAGAG ACTCAGCAAC AGTCACAGAC AGAAGGGTCA TGTGTTCCIT CCTGGGCAGG 420
GCTGAATGTG GCAGGTGCGG CGTGAGGCT GCGTCCTGCC GGTGTGCTCC CAGGCAAGGG 480
GTACGGGGGG CCGGCTTGCC TGGGTGGGA CCTCAAGTCT GAGGGTGAGG ATGGCTGAAT 540
30 CTACCTCGCT TATGTCTCAG GGACGGTCAC CCATACCTAG GATGACCCCA GCCAGACCCCT 600
AGAAGGTCTG ATGGCCATCC CAAGTNCCCC CGCGAGGAGA AGAGTTCCCT GGCAGGGGTG 660
35 ACACATTCCC GGTCAACAAG CCACAACACA GTGGTGCTG CACTCTCTCA GCTGTTGCCA 720
CAACACTTGG TGCTGGAATT TTCTCCAGT AGTGAACTT TTAAGGGACA CATGAATAAT 780
TTAAAAAGTC ACACAAACT CTACGAAAGG CAGGAATCCT CACTCTGCTG AGAGCTACCT 840
40 CCTGAGATGT CGCTTCCGA CCCCAGCAGA GGCAGGAGC GACATCAGCT CGGCAGGAG 900
ATCCTNGCCA GCGCGAGGGC TGGCTCTGGT TATTATAAAT AATCTAATT AAATACGCAC 960
45 ATACACACAG ATGTCTGCT TCTACCNAAC GCCAAGAAAA GCAGACATTA GCATCACACT 1020
GTCAACACTT CCTCGAGAAC NGAAG 1045

50

(2) INFORMATION FOR SEQ ID NO: 84:

- 55 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2877 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

60 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

| | | |
|----|---|------|
| | GAATTCGGCA CGAGACAAGA TGGCAGTCAA CAGCTTCCCA AAAGATAGGG ATTACAGAAG | 60 |
| | AGAGGTGATC ACAGACATGA AAAGATGCGA GACGCCGGAG ATCCTTACC ACCAAATAAA | 120 |
| 5 | ATGTTGCGGA GATCTGATAG TCCTGAAAC AAATACAGTG ACAGCACAGG TCACAGTAAG | 180 |
| | GCCAAAAATG TGCATACTCA CAGAGTTAGA GAGAGGGATG GTGGGACCAG TTACTCTCCA | 240 |
| 10 | CAAGAAAATT CACACAACCA CAGTGCTCTT CATAGTTCAA ATTACATTTC TTCTAATCCA | 300 |
| | AGCAATAACC CAAGCAAAC TTCAGATGCA CCTATGATT CTGCAGATGA CTGGTCTGAG | 360 |
| | CATATTAGCT CTTCTGGGAA AAAGTACTAC TACAATTGTC GAACAGAAGT TTCACAATGG | 420 |
| 15 | GAAAAACCA AAGAGTGGCT TGAAAGAGAA CAGAGACAAA AAGAAGCAA CAAGATGGCA | 480 |
| | GTCAACAGCT TCCCAAAGA TAGGGATTAC AGAAGAGAGG TGATGCAAGC AACAGCCACT | 540 |
| 20 | AGTGGGTTTG CCAGTGGAAT GGAAGACAAG CATTCAGTG ATGCCAGTAG TTTGCTCCCA | 600 |
| | CAGAATATTT TGTCTCAAAC AAGCAGACAC AATGACAGAG ACTACAGACT GCCAAGAGCA | 660 |
| | GAGACTCACA GTAGTCTAC GCCAGTACAG CACCCCATCA AACCAGTGGT TCATCCAACT | 720 |
| 25 | GCTACCCCAA GCACTGTTCC TTCTAGTCCA TTTACGCTAC AGTCTGATCA CCAGCCAAAG | 780 |
| | AAATCATTTG ATGCTAATGG AGCATCTACT TTATCAAAC TGCCTACACC CACATCTTCT | 840 |
| 30 | GTCCCTGCAC AGAAACAGA AAGAAAAGAA TCTACATCAG GAGACAAACC CGTATCACAT | 900 |
| | TCTTGCACAA CTCCTCCAC GTCTTCTGCC TCTGGACTGA ACCCCACATC TGCACCTCCA | 960 |
| | ACATCTGCTT CAGCGGTCCC TGTTTCTCCT GTTCCACAGT CGCCAATACC TCCCTTACTT | 1020 |
| 35 | CAGGACCCAA ATCTTCTTAG ACAATTGCTT CCTGCTTTGC AAGCCACGCT GCAGCTTAAT | 1080 |
| | AATTCTAATG TGGACATATC TAAATAAAT GAAGTCTTA CAGCAGCTGT GACACAAGCC | 1140 |
| 40 | TCACTGCAGT CTATAATTCA TAAGTTTCTT ACTGCTGGAC CATCTGCTTT CAACATAACG | 1200 |
| | TTCTGTGATT CTCAAGCTGC TCAGCTCTCT ACACAAGCCC AGCCATCTAA TCAGTCTCCG | 1260 |
| | ATGTCMTTAA CATCTGATGC GTCATCCCCA AGATCATATG TTTCTCCAAG AATAAGCACA | 1320 |
| 45 | CCTCAAACCT ACACAGTCCC TATCAAACCT TTGATCAGTA CTCCTCCTGT TTCATCACAG | 1380 |
| | CCTAAGGTTA GTACTCCAGT AGTTAAGCAA GGACCAGTGT CACAGTCAGC CACACAGCAG | 1440 |
| 50 | CCTGTAACTG CTGACAAGCM GCAAGGTCAT GAACCTGTCT CTCCTCGAAG TCTTCAGCGC | 1500 |
| | TCAAGTAGCC AGAGAAGTCC ATCACCTGGT CCCAATCATA CTTCTAATAG TAGTAATGCA | 1560 |
| | TCAAATGCAA CAGTTGTACC ACAGAATTCT TCTGCCCGAT CCACGTGTTT ATTAAGCCCT | 1620 |
| 55 | GCACTAGCAG CACACTTCAG TGAAAATCTC ATAAAACAG TTCAAGGATG GCCTGCAGAT | 1680 |
| | CATGCAGAGA AGCAGGCATC AAGATTACGC GAAGAAGCGC ATAACATGGG AACTATTAC | 1740 |
| 60 | ATGTCCGAAA TTTGTACTGA ATTAAAAAT TTAAGATCTT TAGTCCGAGT ATGTGAAATT | 1800 |

| | | |
|----|--|------|
| | CAAGCAACTT TGCGAGAGCA AAGGGATACT ATTTTGTGAGA CAACAAATTA AGGAACTTGA | 1860 |
| 5 | AAAGCTAAAA AATCAGAATT CCTTCATGGT GTGAAGATGT GAATAATTGC ACATGGTTTT | 1920 |
| | GAGAACAGGA ACTGTAAATC TGTGCCCCAA TCTTAACATT TTTGAGCTGC ATTTAAGTAG | 1980 |
| | ACTTTGGACC GTTAAGCTGG GCAAAGGAAA TGACAAGGGG ACGGGGTCTG TGAGAGTCAA | 2040 |
| 10 | TTCAGGGGAA AGATACAAGA TTGATTGTGA AAACCCCTGA AATGTAGATT TCTTGTAGAT | 2100 |
| | GTATCCTTCA CGTTGTAAAT ATGTTTGTGA GAGTGAAGCC ATGGGAAGCC ATGTGTAACA | 2160 |
| 15 | GAGCTTAGAC ATCCAAAAC TATCAATGCT GAGGTGGCTA AATACCTAGC CTTTACATG | 2220 |
| | TAAACCTGTC TGCAAAATTA GCTTTTAA AAAAAAAAAA AAAAAAATG GGGGGTTAA | 2280 |
| | TTTATCATTC AGAAATCTTG CATTTTCAAA AATTCAGTGC AAGCGCCAGG CGATTTGTGT | 2340 |
| 20 | CTAAGGATAC GATTTTGAAC CATATGGGCA GTGTACAAAA TATGAAACAA CTGTTTCCAC | 2400 |
| | ACTTGCACCT GATCAAGAGC AGTGCTTCTC CATTTGTTT GCAGAGAAAT GTTTTTCATT | 2460 |
| 25 | TCCCGTGTGT TTCCATTTC TTCTGAAATT CTGATTTTAT CCAITTTTTT AAGGCTCCTC | 2520 |
| | TTTATCTCCT TTCTTAAGGC ACTGTTGCTA TGGCACTTTT CTATAACCTT TTCATTCTG | 2580 |
| | TGTACAGTAG CTTAAAATG CAGTGATTGA GCATAACCTA CTTGTTTGT TAAATTATTG | 2640 |
| 30 | AAATCCATTT GCACCCTGTA AGAATGGACT TAAAGTACT GCTGGACAGG CATGTGTGCT | 2700 |
| | CAAAGTACAT TGATTGCTCA AATATAAGGA AATGGCCCAA TGAACGTGGT TGTGGGAGG | 2760 |
| 35 | GAAAGAGGAA ACAGAGCTAG TCAGATGTGA ATTGTATCTG TTGTAATAAA CATGTTAAAA | 2820 |
| | CAAAAAAAAA AAAAAAAGG CGCGGGCTCG CGATCCTAGA ACTAGCGGAC GCGTGGG | 2877 |

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(2) INFORMATION FOR SEQ ID NO: 85:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1367 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

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- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

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| | | |
|----|---|-----|
| | AATCATGAGC CTCCAGAAGA GACAGATGGC CCACCAGGAG CTGTTGCTCT GGTGCTTC | 60 |
| | CTGCAGGCCT TGGAGAAGGA GGTGCCATA ATCGTTGACC AGAGAGCCTG GNAACTTGCA | 120 |
| 55 | CCARAAGATT GTTGAAGATG CTGTTGAGCA AGGTGTTCTG AAGACGCAGA TCCCGATATT | 180 |
| | AACCTACCAA GGTGGATCAG TGAAGCTGC TCAGGCATTC CTGTGCAAAA ATGGGGACCC | 240 |
| 60 | GCAGACACCT AGATTGACC ACCTGGTGGC CATAGAGCGT GCCGAAGAG CTGCTGATGG | 300 |

CAATTACTAC AATGCAAGGA AGATGAACAT CAAGCACTTG GTTGACCCCA TTGACGATCT 360
 TTTTCTTGCT GCGAAGAAGA TTCCTGGAAT CTCATCAACT GGAGTCGGTG ATGGAGGCAA 420
 5 CGAGCTTGGG ATGGGTAAAG TCAAGGAGGC TGTGAGGAGG CACATACGGC ACGGGGATGT 480
 CATCGCCTGC GACGTGGAGG CTGACTTTGC CGTCATTGCT GGTGTTTCTA ACTGGGGAGG 540
 CTATGCCCTG GCGTGGGCAC TCTACATCCT GTACTCATGT GCTGTCCACA GTCAGTACCT 600
 10 GAGGAAAGCA GTCGGACCCT CCAGGGCACC TGGAGATCAG GCCTGGACTC AGGCCCTCCC 660
 GTCGGTCATT AAGGAAGAAA AAATGCTGGG CATCTTGGTG CAGCACAAG TCCGGAGTGG 720
 15 CGTCTCGGGC ATCGTGGGCA TGGARGTGA TGGGCTGCC TTCCACAACA MCCACGCCGA 780
 GATGATCCAG AAGCTGGTGG ACGTCACCAC GGCACAGGTG TAACCGTCCA TGTTCCTGT 840
 GAGCAGAGTC CCTACCAACG GGCAGGTCTG CATCCGGGGA GAATGCAGCT GCTTCTGGCG 900
 20 ACAATCCTGC TAGTAAACAC TGGTCTTCGG TGAGCAACGA AACTCGCCT GGCCTGGGAA 960
 ACTGCATGCC CACTTCTCGG GAGGGGTAG TGCAGGTGCC GTGGACAAAG GACAACATTT 1020
 25 CTCTGGGGCT TTTTAACTTT TATTCCTAAG ACTCTAAAGG CGTTGATTTC AACCCCTCCTT 1080
 CACTCTGGCT TCTTCAGGCA ACCCAGTGG TCTCCTGTGA GAATCTTCTC GACAGTTACT 1140
 TATGGGGACA CTGTGAACA ATTAAGTCC AGGCAGAGCA TGAGAACAA CATTCCCAGG 1200
 30 CCATGTAGGA TAGGATACTC CAGACTCCAG TCATCCTCCC CCATCCATGG TTTCTGTTAC 1260
 TCATGGTTTC AGTTACTCAT AGCCAAGTGC AGACCGAAAA TACTAAATGA AAAATTTTCA 1320
 35 AATAAACAA CTCTTAAGTT TTAACAAAAA AAAAAAWAA ACTCGTA 1367

40 (2) INFORMATION FOR SEQ ID NO: 86:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1009 base pairs
 (B) TYPE: nucleic acid
 45 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 86:

50 GAATTCGGCA CGAGCTCGTG CCGAATTCTC GTGCCGAAC TAAACGTATC AAGAAATACC 60
 TGGGCTTGAA GAATATTCAC CTGAAATATA CCAAGAAACA TCCCAGCTTG AAGAATATTC 120
 ACCTGAAATA TACCAAGAAA CACCGGGGCC TGAAGACCTC TCTACTGAGA CATATAAAAA 180
 55 TAAGGATGTG CCTAAGAAT GCTTTCCAGA ACCACACCAA GAAACAGGTG GGCCCCAAGG 240
 CCAGGATCCT AAAGCACACC AGGAAGATGC TAAAGATGCT TATACTTTTC CTCAAGAAAT 300
 60 GAAAGAAAAA CCCAAGAAG AGCCAGGAAT ACCAGCAATT CTGAATGAGA GTCATCCAGA 360

5 AAATGATGTC TATAGTTATG TTTTGTTTTA ACAATGCTCA ACCATAAAGT TGTGGTCCAA 420
 TGGAACATAC AGCTTAATAG TTTATGCGTG ATTTTCTCAA AATATTGTAA AACTTTTGAC 480
 AATGCTCATT AATATTATTT TTTCTATTTG TAGACCATAT CTGAAAGAAA TAACATTTTT 540
 TAAGGCTCTA CCACATAGAC AATATCATGC TAGAATGTGT GTGTGTGTGT GTGTGTGTGT 600
 10 GTGTGTATGT ATGTATAGGT CGGGGAGAGG ATAGTGGTGG GAACAGACAA ATAAGGAAGC 660
 GGGGAGGACT GGATAATTGG TTTTCCCCC TAAGAACATT TATTTACGTC TTAAGAGCAG 720
 ATAAGTGACT AAGACTGAAC ACATACATTT TGTGGAGTAT ATAGTTTTCT TGTAAATGCT 780
 15 GTTCAATTAT TAATGTAACA GTAGCATCAA AATTTTATTC AGGCTTTAGT TGACTCTTTT 840
 GGTCAAGTTT AACAAATCTC CTTAAAAGAT ATTTTGGAGT GATGAATGTA GTTTACTTTT 900
 20 GTATTTGAAT TTTGATTTTC TATTTTTATT TTTTAAATAT TGTATTGTG CACAATGTAC 960
 ATTAAATCAT TATTACATGC TTAAAAAAA AAAAAAAA AAAACTCGA 1009

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(2) INFORMATION FOR SEQ ID NO: 87:

30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1367 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 87:

AATTCCAAAA CAAGGTAAAA GGAACCAGAA AAGAAAAAA ATGTAAATAA AGTTATAAAA 60
 ATAAAGAATT TTTTCAAGGT TAAAAAGCTG AAAAAGAAAT AATTTTATAT AAGAAAGAAT 120
 40 TTTATATGGT AAATTTAGTC CTAAATAAAA ATAAGTGGTT GTTTAACAAG GAGGGATGTT 180
 CAGGACAAAC CAGAAAGTCC AAGCATGTCA TGAACATTGG TGTAAATCAT GATAAGATTT 240
 45 TATATATATA TATACACACA CACACACACA CCCCAAAAGC TTTTATATAA TCAAGTTGTC 300
 MTATTATTAT TAAGTTTGG TTTGCTTAGG GAAGAAAGAR CTAATTTTAA AAAAATCAAG 360
 GTTATTACAT CCATGTATCT TCCTGTGTAT GCTTTTAAAG TCCTTGTAAC ATTGAGTTAC 420
 50 AGGGCTTTAA CTCCTGTGTC TGAAAAATCA CAAACACTGA TGACAATCAA AGCCTCATCT 480
 TAAGGCCCCG TAGAAGATGC CAATCAAAAT AACTGCATT CCTGAGGCAC TAGGCAAGAA 540
 55 ATTAAAGCTA TTCAACTCCT CAAGGCCAG GGAAGAGTG GGCAGGTAAG 600
 ATTGTAAGGG CCGATTTTGA AAGATCCAGT AAGTTCAGTT TCTCTATGAA CTAATCATTC 660
 AAGTCAAAGG CAACTGATG CAAAATCAGT ATATGGACCC CTGTGTCTGA TTAGCAAGGT 720
 60

TTTCTTGAAG CATTAACCAA CTCCTTCATA AAGGTTATAA AAGGCTTATG GRAGTTATAT 780
 TTTATAATCA AGATTAAATC TTATAGTTTG TTTACAAAT TTTGAAAATC AAATGTGATT 840
 5 GGCTTCAGGC TGTTTTTATT AGGGCTTCTT GTTTAGAAAG TTAAGTCACC TCTCTCAAAG 900
 AATGAAGGTT TTTGCTTTTT TTGAAATCCT TGAATTATCA CTGGGRTTAA ATAAATGACT 960
 10 TTACGATGAC CTGTAATTTT ATTTTGTAAT GTCAAGTGT TTAACCTTT TGTATTTGAC 1020
 AAGCTTTCCA AAATCAAATT ATAAATTATG TATTTTCTA ACCTAATTAA TCCTTTAAGA 1080
 TCTTAGTTTC CCTAAAGTCC TAAAATGACA TAATTTGGCT TATTTGGTAT AAAAATTATA 1140
 15 TAGGAAGCAT TGTCAAATGT GAAATGGTGT TTGGTTTCT TTGGGCTGTA TTTGTATAAA 1200
 TATGTTATTG GTGTATGTC CAAAATTATG TGAACTCCT ATAATTCTAA TATAACTTAG 1260
 TGTACATTAT CAGTAATAAT CATAATTGTT ATATTAAAT TATGTGTGC CACAGAGGTA 1320
 20 AAAAAAAGG AATTCGATAT CAAGCTTATC GATACCGTCG ACCTCGA 1367

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(2) INFORMATION FOR SEQ ID NO: 88:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1088 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 88:

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GAATTCGGCA CGAGTGAAAT TTTGTCGATT TCAAAAATGG AAAATACATA ATATGCCAGG 60
 CACTTCCTGG GCAATACAGA TACCTGCAGT AATGGAGTGA GCACCAGCAT CTTCCCTGAT 120
 GGCGTGTGCA GTGAGGTGAC TCGTCTGTAG TGTCTCAAG GTCACGTAGA GAGCATACAG 180
 TAAATACTTG TTGACTCTTT CAACTTAAG TTAATGATAC AGTCAGGACT GATAGCCATT 240
 TTGTTGTCCT TCTTGAAAGT TTACGTGGAA GGCAGACCTT GTGTATGCTT TTCAAAGGGG 300
 CTCMTTAGC GCACTTGGCG CTTAAGAATT TGAGATCAGT AAGTGTGATG GTCCTAATCT 360
 TTTTTAAAA GTATTGGAAG TTTGAACYCM CCTGATGGGG TTGGTTTTTT TTTTTTTTTT 420
 TTCCAAAAA ATAATCATTC AAAATAATCG GTTAACATTT TCAATAAGAG CATTACATAC 480
 AAGGAGTTAG GGAACAAAGA GTTTTAAAT CTGGCTCTTT TTATCTCTAC TTAGGGCGTG 540
 CATCTCTCT TCTTACCCCA ACATATACTG ACTTTTTTAGG ACCTCCTTTA GGGAGATCTC 600
 AATATCCCGA ATTTTCTGT GTGGAGAGGG GAAGGAATAT GTCTTTTTTT GCTTTGGTCA 660
 GAGTGGATAC ATTTTATAGT TTGTTTTTTC AAAGACGGGT CTTCTGAGTC ASTTCTTTCA 720
 CTGCTGCCGT AAAGAACTG TATAAAGGTG ATTGAGCAGT GAAGGCATGG ATAAAAGGGG 780

AAATFTTCAG CAGTTCTGAA CGTGCATGTC ATCAAATATA AAGGAGTGAG AACTTGATGT 840
 5 ATAAGAAAAA ATGGAAGTTA AAAAAAWAA AAATCCAAGA ATGGGCTGCT TGTTCAGTA 900
 GTGAACCTCT CGCTGGAGGT ACTAGAGCGG AGTCTGTCTC AAGGATGCTA TTGGAAGCAC 960
 CCCAGCTGTG GGTGGAAAAC TGCACCTTCT GAGCCTAGTC TTTTATAGCC TGGRGTTTTT 1020
 10 GATGCTGATG CTTTTACTAC TTGTTCTTAG ACTWTTTTGC CATACGCTGC TCTGTTTTCT 1080
 CACCTCCA 1088

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(2) INFORMATION FOR SEQ ID NO: 89:

(i) SEQUENCE CHARACTERISTICS:
 20 (A) LENGTH: 1861 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 89:

TCTCTGCCCC TCATCTTGGT AATTAGCCAG CTCAGATAC TTCTGTGGGC CCTGAAGTGG 60
 ACTCTCAAGG TCAGACCAAG GTTGCTGATC TCAGTCCCAC TGTCTTCAGC CAGCTGAAGC 120
 30 TGTGGGGCTG GGCTGGCAGC TTTATGTCA TCTTGCTTCA CCATTTTTTT TTCTCTCTCT
 TTTTATTCTA TTTTAAGTTT AGACCAAAAA AATACAGAGT CATCCCCTAC CCCCACCCCT 240
 35 CTAGAGACCC TCCAGCTAAA AACAGAGCCT GAGTTCAGGG ACCCAAGTGG TGAGCGGCGT 300
 CTTTTGGGGG TGAGGGAGCT TGGGTAGATG AGGCTCCTGG CTGAGCCCTC CCTGTGGTGA 360
 TCCCAGCCTA AGATGGCCCC TCTTCCCTCC TGGTGGGAGA CAGAGGACTG GACCCTGGGT 420
 40 CTCAGGTTCC AGCAAGTCAG GCTAGGGACC TGGGGGGAGG AGACCCATGG ACTTCACCCA 480
 TACTCAGTGA GGGGGCTCCT GCCGTCTGA CGCCACCCCG CCCCATCAGC ACTTAAGCCA 540
 45 CATGACACAA AGTCTGTACC GCACGGGAAA TGTTACGCG CCTGGGCCGT GTGCATGGCC 600
 TCCCGGGCTG TGGGGCAGCC GCATCTGTGA GGTGACYCGT GAAAGTAGGT GATTCCYTTG 660
 CAGAACTTCA GGGACTGGGA GCAGAGGCC CTCACTCAAC GACGTTTGTG CGACATAGTA 720
 50 TTGTATCCAC CTTAGTATTG TATCGAGCCT TTTCTGTGTT TTAATGAGAA AGCAGAACAC 780
 TAGTTTCCTA TTTAAGACTT TAAGGGTTTG TGGGGCGGG CGGGATTAAAC ACAACATTTG 840
 55 GCTTTGTTTT CTTTTCTCTT TGATTTCCAC ATCAGGTGTG TCGAGTGTG TGTGTGTGGA 900
 GATGTTAAGA GCCTCACAAG GAAACTGGGT TATTGGAGGC CAAGGCGGCT TACAGTTCTC 960
 TCGGTTCGTC ACTTAATTCC TGAATGTTTC AGAGAAACAG GAATCAGAAA ATAGCAGATA 1020
 60

TCATGTAGGA AAGAGAGGAT AAACAAAGAA AAAAGAAAA AAAATAAGCT CATACCCAAA 1080
 TTCACAAAGC CTATTTT TA AACCAAAGCA CATTITGAAT GAGTATGGAA CCTCCATGGG 1140
 5 CTCAGAAAAA AGATGCTAAT ATATTTATCT CATTGTTTAC ATAAGCTTTT ACAGTTTCAG 1200
 ACCTCAGCAG CTGTAAGGCC AGTCCAGGA ACCCTCCCCT GCTGCTGGAA ACCCTTCTGA 1260
 10 GTTGGCCCTG GAGTGGCTCA SGGGCAGAGA AGGGTAGCCC TGGGGCTGGG GGAGGGATTG 1320
 GAAGCCTCCC TGGAGTCACC TGAGCCCTCG TCCCATTCC CAGGGCCCT CCAAGCCCAG 1380
 CTGGCACCAA ARAGCTTGGG CCCGTCTGA CCAGCCCCA AGGCCCTCTG GCCGGACCAT 1440
 15 GCTGGTCTG ACCAGCTAGC CTACGCGGG ATGGCCGTC GTTCTGGCCA CAGGACCCGA 1500
 GTCGGGCTT GGTCCCCCT GCTGCTCTGC CCGTGACCT TGGGGATGG TTGATGOGAG 1560
 GGTCCCACTC AAGCCAAAA GCCGGACCT TTGCGCAGCT CTGTCGACTC TGGTGGGTCC 1620
 20 CCACTCTCGG GGGCCCTAA CCCCACCCA GGCAGCGAA GGGGCTGACT GGTCTGGTC 1680
 CTTACCAACA TAGACGTGC AACACTCTT AACAGTGTG TTTTGTATC AATATGTTG 1740
 25 TGCAGTGATG AATGTATTTA TTCTCAGAC TTGGGGCGAG TGAGCGGGTG GCAGGCCGGC 1800
 TCCGCCACTG CAATGCTCCC GCGGACCGA GCCCAGCAA GGGCTCTCC AGGATTGCAA 1860
 A 1861
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(2) INFORMATION FOR SEQ ID NO: 90:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1259 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 90:

AATTCGGCAC GAGCTCGTGG AGAGATTGAA GATGGCGGCT TCTCAGGCGG TGGAGGAAAT 60
 45 GCGGACCGCG TGGTTCTGGG GGAGTTTGGG GTTCGCAATG TCCATACTAC TGACTTTCCC 120
 GGTAACATTT CCGTTATGA TGATGCCTGG GACCAGGACC GCTTCGAGAA GAATTTCCGT 180
 50 GTGGATGTAG TACACATGGA TGAAACTCA CTGGAGTTTG ACATGGTGGG AATTGACGCA 240
 GCCATTGCCA ATGCTTTTCG ACGAATTCTG CTAGCTGAGG TGCCAATAT GGCTGTGGAG 300
 AAGGTCTCGG TGTACAATA TACATCCATT GTTCAGGATG AGATTCTTGC TCACCGTCTG 360
 55 GGGCTCATTC CCAITCATGC TGATCCCCGT CTTTTTGAGT ATCGGAACCA AGGAGATGAA 420
 GAAGGCACAG AGATAGATAC TCTACAGTTT CGTCTCCAGG TCAGATGCAC TCGGAACCCC 480
 60 CATGCTGCTA AAGATTCTCT TGACCCCAAC GAACTGTACG TGAACCACAA AGGCTGATCT 540

5 MTTTCAGAG GGCACATCC GACCAGTGA TGATGATATC CTCATCGCTC AGCTGCGGCC 600
 TGGCCAAGAA ATTGACCTGC TCATGCACTG TGTCAAGGGC ATTGGCAAAG ATCATGCCAA 660
 GTTTTCACCA GTGGCAACAG CCAGTTACAG GYTCTGCCA GACATCACCC TGCTTGAGCC 720
 CGTGAAGGG GAGGCAGCTG AGGAGTTGAG CAGGTGYTTC TCAMCTGGTG TTATTGAGGT 780
 10 GCAGGAAGTC CAAGGTAAAA AGGTGGCCAG AGTTGCCAAC CCCCAGCTGG ATACCTTCAG 840
 CAGAGAAATC TTCCGGAATG AGAAGCTAAA GAAGGTTGTG AGGCTTGCCC GGGTTCGAGA 900
 TCATTATATC TTCTCTGTG AGTCAACGGG GGTGTGCCA CCAGATGTGC TGGTGAGTGA 960
 15 AGCCATCAAA GTACTGATGG GGAAGTGCCG GCGCTTCTG GATGAACTAG ATGCGGTTC A 1020
 GATGGACTGA GCTTGATGC TTCTGAGGCA AGCTGAAGCT TTGGGTTCTG ACTGACCCAC 1080
 20 CCTACAGGAC TGCTGAACAG AGAGCCCACT GTGACTAGGG ATCCTGAGTT TTCTGGGACA 1140
 ATTCCAGCTT TAATCAATAC ATTTGTATA ATGTGCCATA AAATGAGACT TTTTACGCCT 1200
 25 TTATAAGGCC TTAGATGTAA ATAACTCAC CCAACAAAA AAAAAAAAAA AAAACTCGA 1259

(2) INFORMATION FOR SEQ ID NO: 91:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1566 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

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(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 91:

40 CTAGAAGAGC AAGCCCCCA GNANTGATGA AAAGTGATT TCCTGGAGAC CTTGGCAGTC 60
 AGCGACAAGC TATTCCAACA ACTAAGAGAT CAGGACTCCA GTAGCAGTGA GTTCTGCACC 120
 TTCTGGTGAC AGTGAGGGTG ATGAAGAGGA GACGACACAA GATGAAGTCT CTTCCACAC 180
 45 ATCAGAGGAA GATGGAGGGG TGGTCAAAGT GGAGAAAGAG TTAGAAAATA CAGAACAGCC 240
 TGTGTTGGG AACGAAGKT TAGAGCACGA GGTACAGGG AATTGAATT CTGACCCCTT 300
 GCTTGAATC TGCCAGTGT CCTCTGCCA GCTAGACTGC GGGACCGGA GCAGTTGATT 360
 50 GCTCACGTGT ACCAGCACAC TGCAGCAGTG GTGAGCGCCA AGAGCTACAT GTGCTCTGTC 420
 TGTGGCCGGG CCTTAGCTC CCGGGGTCA TTGGGTGCC ACCTCTTAAT CCACTCGGAG 480
 55 GACCAGGAT CTAAGTGTG TGTGTGTGA GCGCGTTCA CCAGCCATGC CACTTTTAAC 540
 AGTGAGAAAC TTCCTGAAGT ACTAAATATG GAATCCCTAC CCACAGTCCA CAATGAGGGT 600
 60 CCTCCAGTG CTGAGGGGAA GGATATTGCC TTAGTCCTC CAGTGATCCC TGCTGGAATT 660

| | | |
|----|---|------|
| | CTGCTTGTTGT GCAACAACCTG TGCTGCCTAC CGTAAAMTGC TGAAGCCCCA GACTCCCACT | 720 |
| | GTASGCAAGT GGGCTCTACG TCGACAGAAT GAGCCTTTGG AAGTACGGCT GCAGCGGCTG | 780 |
| 5 | GAACGAGAGC GCACGGCCAA GAAGAGCCGG CGGGACAATG AGACCCCGA GGAGCGGGAG | 840 |
| | GTGAGGCGCA TGAGGGACCG TGAAGCCAAG CGCTTGCAGC GCATGCAGGA GACAGACGAG | 900 |
| 10 | CAGCGGGCAC GCCGGCTGCA GCGGGATCGG GAGGCCATGA GGCTGAAGCG GGCCAATGAA | 960 |
| | ACCCCGGAAA AGCGGCAGGC CCGGCTCATC CGAGAGCGAG AGGCCAAGCG GCTCAAGAGG | 1020 |
| | AGGCTGGAGA AAATGGACAT GATGTTGCGA GCTCAGTTTG GCCAGGACCC TTCTGCCATG | 1080 |
| 15 | GCAGCCTTAG CAGCTGAAAT GAACTTCTTC CAGCTGCCTG TAAGTGGGT GGAGTTGGAC | 1140 |
| | ARCCAGCTTC TGGCAAGAT GGCCTTTGAA GAGCAGAACA GCAGYTYTCT GCACTGAACC | 1200 |
| 20 | ACACCCCTCT GCCTGCCCTC CTTCCACCT ACCTACCCAC CCACCCACAC CCACAGCCAC | 1260 |
| | GAGGACCACT GCTGCTGCCA CCCACGAGGC CTTGTCCTTG CTGCCAGAGG CAGGCCTGGG | 1320 |
| | TTTATTGCAG GTGACCTGA GCAGCCCTTG CATATGGGAA CAGGATGATG GGGTCAGGAG | 1380 |
| 25 | GGACCTGGCT CAAGGCAGCT CTGGACAAGG GAGCAGGCAG TCCAGAGAAC TGGCCTCCCC | 1440 |
| | AGCCCACTGC CACAGGCTGT GCTTCTAGGA CTGTGGGCC CTGTGTGGCC CATGAAGTTG | 1500 |
| 30 | TGAAGTCAAA TAAATTAATT TTATCTTTAA AAAAAAAAAA AAAAAAYYGG GGGGTTTTTT | 1560 |
| | TGGGGG | 1566 |

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(2) INFORMATION FOR SEQ ID NO: 92:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 1593 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 92:

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| | | |
|----|---|-----|
| | GGCAGAGCC TCGGCTCGG TGGCGGTGGT GGACACGTCG AGCGGGTAG AAGTGGAGGG | 60 |
| | GCCGTTGAA GAGTCGTGAG GGGGTGACGG GTTAAGATTC GGAGAGAGAG GTGCTAGTGG | 120 |
| 50 | CTGGACTTGA CCTGAAAGA ATCTTCTGCT GACTCTCAAC TTTCTCTGGA AAAAATGGAT | 180 |
| | CATTCCCACT ATATGGGGAT GAGCTATATG GACTCCAACA GTACCATGCA ACCTTCTCAC | 240 |
| 55 | CATCACCCAA CCACTTCAGC CTCACACTCC CATGGTGGAG GAGACAGCAG CATGATGATG | 300 |
| | ATGCCTATGA CCTTCTACTT TGGCTTTAAG AATGTGGAAC TACTGTTTTT CCGTTTGGTG | 360 |
| | ATCAATACAG CTGGAGAAAT GGCTGGAGCT TTTGTGGCAG TGTTTTTACT AGCAATGTTT | 420 |
| 60 | TATGAAGGAC TCAAGATAGC CCGAGAGAGC CTGCTGCGTA AGTCACAAGT CAGCATTCGC | 480 |

TACAATTCCA TGCCTGTCCC AGGACCAAAT GGAACCATCC TTATGGAGAC ACACAAAAC 540
 GTTGGGCAAC AGATGCTGAG CTTTCCTCAC CTCCTGCAAA CAGTGTGCA CATCATCCAG 600
 5 GTGGTCATAA GCTACTTCCT CATGCTCATC TTCATGACCT ACAACGGGTA CCTCTGCATT 660
 GCAKKAGCAG CAGGGGCCGG TACAGGATAC TTCCTCTTCA GCTGGAAGAA GGCAGTGGTA 720
 10 GTGGATATCA CAGAGCATTG CCATTGACAT CAACTCTAT GCGTGGCCT TATCGATTGC 780
 AGTGGGAAGT TGTGAAGAC TTGAAGACGT GATTCTGCT CCAATCATCC CTTCTTGCTC 840
 CTCTTTGKGC ACGTACACAC ACACACACAC ACACACACAC ACACACCCGT GYTCAAACAG 900
 15 AGGTTTAGTT TACAGTCTCT GAACTAAAGT AGTAACCTCC CAAATTGTTT TTTCTAATAA 960
 GCTGAGATTC CCATTTCTCT TAAGGAGAAG CCACCCATGA GATGTCTTTT CTTCTCCAT 1020
 20 CATCTTAGAG CCAAGTTATA TGTCTTGTC TAATCCATGT AGCTTTTGT TCAATGACTT 1080
 GATCATCTGC TTCCTTTTGG AATTTTAAAC AGATAGTAAG TAAATTGGT GGTTTTTC 1140
 CCTGGGTCAG TGATGAAAG GGGTTAACTT CAGCCAGGAT TGATGGCAGC TGAGGAAAT 1200
 25 TCTTGCCCAA CTAAACCCAG AACTCAAAC TAACATTAGA AAATAAGGTC CAGGGCCGA 1260
 CACAGTGGCC CAAGCAAGTA ATCCAGCAC TTGGGGGGC CAAGGCAGC TGGATCACCT 1320
 30 GAGGACAGGA GTTCGAGACC AGTCTGGCCA ACATGGGAA ACCCGTCTC TACTAAAAAT 1380
 ACATAAATTA GCCGGCATG GTGGTGGCG CCTGTAATCC CAGCTACTCA GAAGCTGAG 1440
 GCAGGAGAAT CACTTGAACA TAGGAGCGG AGGTGTCAGT GAGCCAAGAT GGCGCCATTG 1500
 35 CACTCCAGCC TGGGTGACAA GNGTGAACT CCATCTCATA AAAAAAAAAA AAAATANTCG 1560
 AGGGGGGGCC CGGACCCAA ACGCCGAAA GTG 1593
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(2) INFORMATION FOR SEQ ID NO: 93:

- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 970 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 93:

CTCGTGCCGA ATTGGGCAG AGGTGCCAG GCTCTCAGG CAGAGGTCC AGTGTGATCA 60
 55 CTTTGCATGG CCTCTCTCC CTCCTGAGCT TGTGCCAGG CCCCAGGGCT GACCTGGAGA 120
 GGAAAWGCC AGAGGTGAA GATGGGTGT CTGGTTTGG GACCATCCTG GCCCCCTTG 180
 TCACTGTTGG CATCTCTTCT GCACAGTGGC ATTGCTGGGA GTGCTTACT GTGCCTATTC 240
 60

AAGGGGCTGG CAGCCGACG CTCACTGCAG ATCAGGGACT TGGCTTCCCG GTTGACCACA 300
GGTCCAAGAA CCTGCAGGT CCAGCTCCC CCCCATCCCC AGTCTTCCCC ACCCTGGCCC 360
5 GGGCCTCCAG GTGCAGAAC ATGCAGGCC CTCTCCAGGA CTGTGGGAGG AGTGTGTCCC 420
TCAGACTGGC CTGTGTCTTG GCTCCTCTTA CCACCTCTTC CAGAGGTTGT CACCTGCAGC 480
TGCCCCAGGA TAAAGGCAAG GCCAGAGAGG ACTCCTGAAC TCCTGTGTGC CTGGGGTGGC 540
10 AGGGGCAAC ATAGCCAACT GGTGGCCTGA GCGGGGCCAT GGTGARGACA CCCTTGGTGG 600
CTTGTCCAC ATCAAGCTGG GARGTGACAC TGAGGATGCA TTAGTCTGCA GCGTATGATA 660
15 AAAACGGCAT TTCAGGCCAG GCGTGGTGGC TCATGCCGTG CACCCAGCA CCTTGGGAGG 720
CCGAGGTGGG CAGATCACAT GAGGTCAGGA CTTTGAGACC AGCCTGGCCA ACATGGTGAA 780
AACTCATCTG TACTAAAAA ACAAAATTA TGTGGGTGG TGGTGTGTGC CTGTAATCCC 840
20 AGCTACTTGG GAGGCTGAGG CAGGAGAATC ACTTGAACCT GGGAGGCGGA GGCTACAACG 900
AGCCGAGATT GCACCACTGC ACTCCAGCCT GATCCGTCTC AAAAAAAAAA AAAAAAAAAA 960
25 AAAAACTCGA 970

30 (2) INFORMATION FOR SEQ ID NO: 94:

(i) SEQUENCE CHARACTERISTICS:

- 35 (A) LENGTH: 934 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 94:

40 TCTCTCTCTC TCTCTCTCTC TCTGCTGTAA AGAACTCCCA AAATCAAAT GTATCAGGAA 60
ATGTAAAGGT TAAGTCTGAC TACAAGAAGG CCAAAATTGC ACCAGCTTCC TAAGTGAAGA 120
ATAATAGAAT AAAACATATA GAGGCGAGAA ATAAAATGAG GTGTATCTGG AGAATTTTAT 180
45 GATGAGCATT TAGATTTAGC AATGCCCAAT GTCATGCTGA CACTGTTTGT CATGACCTTG 240
TCTTCAGCTA GTAATTTGGG GTTGTACTTT TTAAATTTA ATTTTGAATG TTCTTGCATG 300
50 TTTGGTACCT CTCCTCTCAC TGCTAAAGAT AAATGTTTA TCTGTATAAC ATAACTACAC 360
CAATGTCATT TATTGTATAC GCTAGTACAC AAATGTGTTT TTTATTAAG TAATGAARTA 420
TTTGCTGTGA AAAATGTATT ATTTGTGCCA CCGTTTATAT CTGTGTTTAT TTTCTGTGTG 480
55 TATATGCGTG TGTATTCGAA TCTCAATTTT TCTTTTACTC TAGTTTAGAT TAAGACATAT 540
TTAGATGAAA TTTTAAAAAT AACATTGGAA ATAGGAGGCT AAGTTTGTGTT SAGTCTCATT 600
60 CCCTTGGGGG GAAATTGCTT TTGCCATTTT ATTTTCATGT ACAATAACCT AAAAAGGATC 660

TCCTACTGAC TTCCTTCCTA ATTATTATTG TTTTACACGA AAGAAAGGAA ATACGTTTTT 720
 AATTGAGTTG TTTGAAATCA TTCACCTTGT GTAGATTTC CAGACTGATG TTTCATTGTA 780
 5 AGAATATTAC ATTATAGACA GGTGCGCCAT TTCACAAGCA ACTAATCCAT AGTTTTGGAA 840
 GCCCGCTTTA AGAGACCTGA ATATCTTTGT TTTTAATAAA ATACTTAGAG TTTAAAAAAA 900
 10 AAAAAAAAAA AAAAAAAAAA AAAAAAAGG TAAA 934

15 (2) INFORMATION FOR SEQ ID NO: 95:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1392 base pairs
 (B) TYPE: nucleic acid
 20 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 95:

25 CAGCTCAGCT CTGCGCTGCT GCACGCCAAC CACACACTCA GCACCATTGA CCACCTGGTG 60
 TTGGAGACGG TGGAGAGGCT GGGCGAGGCG GTGAGGACAG AGCTGACCAC CCTGGAGGAG 120
 GTGCTCGANC CGCGCACGGA GCTGGTGGNT GCCGCCGAG GGGCTGACG GCAGGCGGAG 180
 30 GCTGCGGCCC AGCAGCTGCA GGGGCTGGCC TTCTGGCAGG GAGTGCSCCT GAGCCCCCTG 240
 CAGGTGGCTG AAAATGTGTC CTTTGTGGAG GAGTACAGGT GGCTGGCCTA YGTCTCCTG 300
 CTGCTCCTGG AGCTGCTGGT CTGCCTCTTC ACCCTCCTNG GCCTGGCGAA CAGAGCAAGT 360
 GGCTGGTGAT CGTGATGACA GTCATGAGTC TCCTGGTTCT CGTCCTGAGC TGGGGCTCCA 420
 TGGGCCTGGA GGCAGCCACG GCCGTGGGCC TCAGTGACTT CTGCTCCAAT CCAGACCCTT 480
 40 ATGTTCTGAA CCTGACCCAG GAGGAGACAG GGCTCAGCTC AGACATCCTG AGCTATTATC 540
 TCCTCTGCAA CCGGGCCGTC TCCAACCCCT TCCAACAGAG GCTGACTCTG TCCCAGCGAG 600
 45 CTCTGGCCAA CATCCACTCC CAGCTGCTGG GCCTGGAGCG AGAAGCTGTG CCTCAGTTCC 660
 CTTCAGCGCA GAAGCCTCTG CTGTCTTTGG AGGAGACTCT GAATGTGACA GAAGGAAATT 720
 TCCACCAATT GGTGGCACTG CTACACTGCC GCAGCCTGCA CAAGGACTAT GGTGCAGCCC 780
 50 TGGGGGGCCT GTGCGAARAC GSCCTGGAAG GCCTGCTCTT CCTGCTGCTC TTCTCCCTGC 840
 TGTCTGCAGG AGCGCTGGCC ASTGCCCTMT GCAKCCCTGCC CCGAGCSTGG GCCCTCTTCC 900
 55 CACCCAGGAA TCCAAGCGCT TTGTGCAGTG GCAGTCGTCT ATCTGAGCCC CTCCTCCCGG 960
 CTGGACTGGA GCCTGGCTCC CCTCTCGTTT CCTCCCTGG CTGCCGGAGA GACCCCACTA 1020
 ACCCAGCCTG CCTGGGCTCT GACCACTAAC ACTCTTGGCC ATGGACAGCC TGCACAGGAC 1080
 60

CGCCTCCCTG CTCTTGGCCA CTGTGCTCCC ATTTCTGTCC TTGGCCTTGG GAGTAGCTGA 1140
 GGGGGCAGAC TAGGGAGTAG GGCTGGCAGG GGAGGGGGCA GACAGCCTCG CCTCGCACCC 1200
 5 TTCACTCCCTG GCTGCCCGTC CCATCCTTGG AGGGACTAAG CTGGGGGTGG GACATGAGTC 1260
 CCCCTGCTGC CCCTGCCACA TCCCAGTGGG CTCTGACCCC CTGATCTCAA CTGCTGGCAC 1320
 10 TAACITGGAA AAGGGTTGAT TTAAAATAAA AGGGAAGACT ATTTTACAAA AAAAAAAAAA 1380
 AAAAAAATC GA 1392

15

(2) INFORMATION FOR SEQ ID NO: 96:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1963 base pairs
 20 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 96:

25 GGTANCTGCA GTACGGTCCG ATTCCCGGGT CGACCCACGC GTCCGGAGAA ATGCAAATTA 60
 AAACAGTAAA GTGTCAATTTT CACTTCCTGG ATTGGCAAAG GGTTTTATGT ATTTTACTGA 120
 30 CAGTGCTCAA CATTAGCAGT AAACAACAAA TGGTGAGTAA ATATGAGCTT CGGAACCTCA 180
 GGGAAATGAT CTCCTTATTT CAACCTGCAG ATTCTTCTCT ACAACCAGTG TAGAGCAGAG 240
 TACCAGGACG GGCCATTGAG CACCCTGGTG TTGAGATCAA GTGGCCTCTA GTCAGAGTTG 300
 35 GGTCAAGGCC ACTGTGAGTG GGCTGCCCCC AACATGAGTC AGCTGTCTAG GACTAGTTTA 360
 TCTCTGCTTC TCACTTTACT GGTATTATGG GGCAGCTCCT GCTGTCTTCC AATTGGTGT 420
 40 CTTCCAAATC GGCACCGTCT TTTAAAGTTG AGTTTCTTGT TATTCTCACC TGATATACCT 480
 TATTTATCCC ACACCCACCC CAATAACATA TCGTGCTCAG TGTATCTTT GAGACAACAC 540
 TTGAATTTTA CTCAGCCTGG AGCGCTCTTC ACATGTCTTG TCCAGATCCA GTTCGGACTC 600
 45 ATTCTTCAGC CGTGATCAG TAAATGGGGG CTAGGTAAA CTGTGGTGAC AAACAACCTC 660
 CAAATTCAG TGGCTCAAAA ATCTTCTTCC TCATTTATWT ACATTTTCATC ATGGGTCAGG 720
 50 TGAGAGGTAG CTCGTGCTG TGTATCCTA ACACAGGAAT CCAGACGAA GGAGGGACAA 780
 TCAATAAGAT CCCCATGCT ATAGAAAAGA RAAAAAGTA TCGGAATAR CACTCYGTTT 840
 CYTGAGAWT YCTCCTGAAA AAGTCACATG TTATTTCTTC TCACCTCCAT TGGCAAAAAA 900
 55 AAAGTCATGT GGCCATGTGA AAATGTAAGT AGGCGGGATG GAACAGTCAG AATGCATTCA 960
 TAAATATGA ACTGAAAATA TCTGGAGAAC ARCACCTATG ACTACCAGGA ATGCCAACAT 1020
 60 GCATCCCTAA CAACCCAGTG CTGTACCCT CCAAACCTTT TATGTCTTGC AAAGTATTAG 1080

| | | |
|----|---|------|
| | AAC TTC T TAT CTGAAGCCAT ACCACTCAGA GGAANGCAA AATACATATT GACATCTCCT | 1140 |
| | TTAGGATGTC CTTAGAGAAT TCAAGGAAAA GAAGTTAAAT AATTTTAAAG TCCTTTTGGG | 1200 |
| 5 | TACAGCTATT TAGCACTAGA GGGTAAGATT AGACATAGAT TGTAAGATA ATNATAGGGT | 1260 |
| | TAGGGATAGG ATTAGGATCT GGGTCAGAGT CAGGCCAGA AGTATGGTTA GAGGTGGGT | 1320 |
| 10 | CATGGTCAGG GTSGAGATCA AAGTCAGGGT CAAAGTAAGG GTCAGAATTA GGGACCCAGG | 1380 |
| | ATAGGGATCA GGATTAGGT TCAGTGTCAA AGTCTTGGGA CAAGGTTAGG GTTAGAATTA | 1440 |
| | GAACCAGAGC TTTGTTCTCC TCAGGACCCA CCCGAGGGTG GGTCAACATG GCTTTGGAGC | 1500 |
| 15 | GCCTGGTAGT GTGGTGTGTC CACAGKGAAG ACCAGAGTTT CATTGTCCTT AAGACTGACY | 1560 |
| | TGGGAGATG TGGCTGTAGS CCATTGAGGA AGGTGAGGCA ACAGCTTCCT GTCTGCTYCC | 1620 |
| 20 | CCGTGTCTG AGGAGGGAGT TCTGCCATGG GCTTTACTTT CACATGTTAT ATTCCACAAG | 1680 |
| | TC TTGTTT TA CAAAAGCATC CCTTCCTTGA GGCTTCGGCT GCTCATCGCT GCTCATCATM | 1740 |
| | ATAGCGTGCC ATAACATATA GTAAGATTG GGT TTGTTT TCGGGAGATA TCTTGGTATA | 1800 |
| 25 | GAGAAAGGAG AAATGCTTAG AGCCACCATC AGGACAGTTG GGATGAAAGT TGGGTATAGG | 1860 |
| | CAGAGGCTGG AGGAAACATG TGCATCCCTT GTAAACACTT TTATTCATGT TTTAATTACT | 1920 |
| 30 | CATTTTCTT ACAGTGTTAA ATTAGTAAAG ATAGTATTGA AAA | 1963 |

35 (2) INFORMATION FOR SEQ ID NO: 97:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 1052 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 97:

| | | |
|----|--|-----|
| 45 | TCATTAAC TT CAGACAACAT CATAAAGCAA TGATAGCTCT TTTCTTTGTG ACCACAAYCT | 60 |
| | TAACTTGAGC TTTGCTGGGT GTTTTGACACA TAACAATGAG GGACTATTAG ACATAACATA | 120 |
| | ATTTTCATAG GTCATTGCCC TGTCAATGAT AGAGAAGATA ATTGCMAGAK AGTTWATTTT | 180 |
| 50 | TGGTGTGTGT ATATGTGCAC AAATGTGCAG GGCCTCTACT TTGCAACTGG AATTTATAGA | 240 |
| | CTAATGATAA AATATATCCC TTAAATATA CAAATGACAA TTGACTTCAA ACTTTCCCAA | 300 |
| 55 | GCCCACATAG AAATTCCTCG AAAACATATA AAATATTGAG TTCTTCAACC TCAGCACTAT | 360 |
| | TGACATTTTG GACCARATAG TTCTGTWGT KAAAGGCKGT CTTTGCACTG TAGAATGTTT | 420 |
| 60 | AGCAATATTC CAGGCCTCTA TCCACCTGAT ACCGGGCTG TATCCCCCTG ATACTGGTAG | 480 |

TTCTTTTTC CCCATCACA AATTGTGACA ACCCAGAAAT ATCTCCTTAT ACCTTTCCAG 540
 AATGTTTTCC CTGGGGGACA AAAAGCACTC CCATTGAAAA ATCCACTGGT CCCAAATGGT 600
 5 TAAAAATTGG TTCCCTTCCC ATTCCTTTTA CCAGGTTTGG GGCCAAGCCC CCTTCCCTTA 660
 ATTTCCCTCC CGAAATGAAC TGAAACCCAA CTGTWACTCT TAATGAAATA TTGAAGGKIT 720
 10 GAAGCTTTAA AAAAAAAAAA AAAAKTACAG CTTGGCTGGG TGCAGTGGCT CAAGCCTGTA 780
 ATCCTAGCAC TTTCGGAGGC CAAGGTGGGC AGATTGCCTG AGCTCAGGAG TTCGACACCA 840
 GCGTGGGCAA CATGGTGAAA CTCTGTCTCT ACTAAAATAC AAAAAGTTAA CCTGGCATGG 900
 15 TGGCAGGTGC CTGTAGTCCC AGCTACTAGG GAGGCTGAGG CAGGAGAATT GCTTGAACCC 960
 AGGAGGCAGA GGTTCAGTG AGCCAAGATT GCCACTGCAC TCCAGCCTGG GCAACATAGC 1020
 AAGACTCTGT CAAAAAAAAA AAAAAAATC GA 1052
 20

(2) INFORMATION FOR SEQ ID NO: 98:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 929 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

30

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:

ATCCATCACA GCCTTCTAT CTAGGCCACA CTATAAAATC TGGAGACCTT GAATATGTGG 60
 35 GTATGGAAGG AGGAATGTG TTAAGTGTAG AATCAATGAA AAGACTTAAC AGCCTTCTCA 120
 ATATCCCAGA AAAGTGTCTT GAACAGGGAG GGATGATTG GAAGATATCT GAAGATAAAC 180
 40 AGCTAGCAGT TTGCCTGAAA TATGCTGGAG TATTTGCAGA AAATGCAGAA GATGCTGATG 240
 GAAAAGATGT ATTTAATACC AAATCTGTTG GGCTTCTAT TAAAGAGGCA ATGACTTATC 300
 ACCCAACCA GGTAGTAGAA GGCTGTGTT CAGATATGGC TGTTACTTTT AATGGACTGA 360
 45 CTCCAAATCA GATGCATGTG ATGATGTATG GGTATACCG CCTAGGGCA TTTGGGCATA 420
 TTTCAATGA TGCATTGGTT TTCTTACCTC CAAATGGTTC TGACAATGAC TGAGAAGTGG 480
 50 TAGAAAAGCG TGAATATGAT CTTGTATAG GACGTGTGTT GTCATTATTT GTAGTAGTAA 540
 CTACATATCC AATACAGCTG TATGTTTCTT TTTCTTTTCT AATTGGTGG CACTGGTATA 600
 ACCACACATT AAAGTCAGTA GTACATTTT AAATGAGGGT GGTTTTTC TTAAAAACAC 660
 55 ATGAACATTG TAAATGTGTT GGAAAGAAGT GTTTAAGAA TAATAATTTT GCAAATAAAC 720
 TATTAATAAA TATTATATGT GATAAATCT AAATTATGAA CATTAGAAAT CTGTGGGGCA 780
 60 CATATTTTG CTGATTGGTT AAAAAATTT AACAGGTCTT TAGCGTCTA AGATATGCAA 840

ATGATAATCTC TAGTTGTGAA TTTGTGATTA AAGTAAACT TTTAGCTGTG TGTTCCTTT 900
ACTTCTGATA CTGATTTATG TTTAACCG 929

5

10 (2) INFORMATION FOR SEQ ID NO: 99:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 359 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
15 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 99:
20 ATNGGANTCC CCCGNGGCTG CAGGAAATC CCCGGGCTGC ATGTCTAGTT CCAGTCTGCA 60
CTGGAAAGAA TTCAAATATG CACCTGGCTC CCTTCACTAT TTTGCCCTAT CCTTTGTGCT 120
CATTTTACT GAAATCTGTC TTGTAGCTC AGGAATGGGA TTCCCCCAGG AAGGAAAGCA 180
25 CTTTCTGTT CTGGGAAGCC CAGACTGTT ACTTTGGGC AGGGACGAAC ATGTGCCTCG 240
TGAATTGCT TGAAAACAGT CACCATCTC TACCCCATC ACTGTATAGT GAAAAACCTG 300
ATTAAAGTGG TATCTGAGAA CCAWAAAAA AAAAAAAA ANCTCGAGGG GGGCCCCG 359

30

35 (2) INFORMATION FOR SEQ ID NO: 100:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 952 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
40 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:
45 GAATTCCTCCG GGGGATCAGG GCAGCGGGG AGGTGGCCAG GCCAGTGGCA GGCCTGTGGA 60
GACAATCCCT YAGGACTAGG GACAGGGCTG TGCCGGCCTG GGCCAGGGCC CACGGACCCG 120
CAGCTCAGGG CGCCTGCCA CGTCGTCTG CGCGGTGCG CCGCGGGCGT CCCTCGCGTC 180
50 TCTTCACTGC ACATTGCAAT GCATTGCGA TTCCCATTTT TCTGCTAGGA GCCAGCCTGG 240
GTTGGCGCTG CTCCAGAGC CGTGGGTCC CAAGANCTTG CGTTCCCTTT TGTTCCTGTC 300
CCGTTTATCA AGAACACGGG CCCACCTGT TCACGTTGCC CGAAGGCCAC CCCAAGCCCA 360
55 ASCCTGCGGG GCGTTCCTM MAYTGCCYTG RAATGCCCGG CTTNAAGTTY TTGCGCAACG 420
CMAGGAATTC AGTGTGGGA CGGCCCTGC CGGATTAGGC YTAGCCCTGG CCCAGGTGGT 480
60 GAGCGGTTG CAGTGTCCT TCTCATCCAC CTGATGGGCC CAGATAAAGG CCCCCGCTGT 540

5 CCAGCCTCCC TGGACGGCCC TCGCGGTCCC TGCAGCCCAA GATGGGACTC AGACCCCTGTG 600
CCCCAGAGCT CCCCTGCCGC AGAATGGGGC CCCAGCCGGC CCGACCGGG TCCAGGAGCA 660
CTGCTCGCCT GTACATACTG TTGCCCTAGC CCACCTGGTG CCGTGGGAGC CACCCCCAGG 720
TGCNTGGCAC AGCCCCCTCC CACTCCGCCA CGCCCCCACC CACCCCGCGT GTTCTGTCCC 780
10 TGTGACTCCT GGAACCTGCG TCCTCCCCAA AGCCATGGGA GGGGTGTCCT CCTCAGACCA 840
TGCCCCCAGA TGATTTTTTT AAATAAGAA ACAAAATGCAC CTGCAAAAMA AAAAAAAAAA 900
15 AAAAAAATC GAGGGGGGGC CCGGTACCCA ATTGCGCCTA TAGTGAGCGA TT 952

(2) INFORMATION FOR SEQ ID NO: 101:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1545 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 101:

30 GAAAGACAAA AGGAAATAGA AGAAAGGGAA AAAAGGCGTA AAGACAGACA TGAAGCAAGT 60
GGGTTTGCAA GGAGACCGAG ATCTCCAACC GGACCTAGCA CGGTGGGCA CAAGATCATG 120
CAGAAGTACG GCTTCCGGGA GGGCCAGGGT CTGGGGAAGC ATGAGCAGGG CCTGAGCACT 180
35 GCCTTGTCAG TGGAGAAGAC CAGCAAGCGT GGCGGCAAGA TCATCGTGGG CGACGCCACA 240
GAGAAAGGTG TGTCCCCAGG GAAGCGTGTG ACTAGAGGGA AAGGACTGGC CCCATCCATA 300
TCAGACATGG CCAGTCTTGA TCCTCATGTG TCAGCAGGGG GACAATGAGG CGTGTGGCCA 360
40 GAGGGAGAGG GCTGGCCCTG CCATCACTAG AACACAGGCC GTCTGTMTCA TATGATGCAC 420
TGCCACTTCC GTTTGTGAA ACCAGGAATC CTGAGGCTCA TCTTTATTTT TTCAGAACAG 480
45 ACGTAGAGAG ATGAAGGCTT GTGGAGGAAA AGATGGTGAG AGACTTGGGC AGAAAATGAG 540
TAGTCCTCAG GAAGAAATCT TGGTTATGTG TTTAGAGCAT GAAGGACAGA GCCATATAGT 600
GTGGCAGTGA ATATACCTGC TATCTCCATC TCAGAGGTG TCTCTACTTT TCCCTTTTGC 660
50 CCTTTCAGTA TAGATGTGAT TTCTGATTCT CTTACAGATT GTTTGCTTTG CGAGATCTGA 720
TGTTATGTTG CAGTCTCTTG GTAAATGATG CCTAGTTGGT GTTTTATTTT CATTTAATTT 780
55 TTACAGTCTG TTCTGTGTTG AGGGAATTCA GGAAAGAGAC AAACATATGT TAGCATTTTA 840
ATCAGGGAAT TAAGTTTGAG TCAGCCTAGC TGAACCTCCT TTGCTAAAGA AAGAAGAAAA 900
60 CTTTCTGCGC AGCCCCGTC ATGCACAGCT TAGGATACAT CACGAGCCTG ACAGATGCAT 960

CCAAGAAGTC AGATTCAAAT CCGCTGACTG AAATACTTAA GTGTCCTACT AAAGTGGTCT 1020
 TACT AGGAA CATGGTTGGT GCGGGAGAGG TGGATGAAGA CTGGGAAGT TGAAACCAAG 1080
 5 GAAGAATGTG NAAAAATATG GCAAAGTTGG AAAATGTGTG ATATTTGAAA TTCCTGGTGC 1140
 CCTGATGAT GAAGCAGTAC GGATATTTTT AGAATTTGAG AGAGTTGAAT CAGCAATTAA 1200
 10 AGCGGTTGTT GACTTGAATG GGAGGTATTT TGGTGGACGG GTGGTAAAAG CATGTTTCTA 1260
 CAATTTGGAC AAATTCAGGG TCTTGGATTT GGCAGAACAA GTTTGATTTT AAGAACTAGA 1320
 GCACGAGTCA TCTCCGGTGA TCCTTAAATG AACTGCAGGC TGAGAAAAGA AGGAAAAAGG 1380
 15 TCACAGCCTC CATGGCTGTT GCATACCAAG ACTCTTGAA GGACTTCTAA GATATATGTT 1440
 GATTGATCCC TTTTATTTT TGTGGTTTTT TAATATAGTA TAAAAATCCT TTTAAAAAAA 1500
 CAAMAAAAAA AAAAAAACT CGAGGGGGG CCCGGTACCC AATTT 1545
 20

(2) INFORMATION FOR SEQ ID NO: 102:

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1322 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

30

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 102:

CTCTCGGGAG CGACCGCTCC GCTCGTCTCG TTGGTTCCGG AGGTCGCTGC GGCGGTGGGA 60
 35 AATGCTGGCG CGCGCGCGC GNGGCACTGG GGCCCTTTTG CTGAGGGGCT CTCTACTGGC 120
 TTCTGGCCGC GCTCCGCSG CGCTCCTCT GGATGCCCC GAAACACCGT GGTACTGTTT 180
 40 GTGCCGAGC AGGAGGCCTG GGTGGTGGAG CGAATGGGCC GATTCCACCG GATCCTGGAG 240
 CCTGGTTTGA ACATCCTCAT CCCTGTGTTA GACCGATCC GATATGTGCA GAGTCTCAAG 300
 GAAATGTCA TCAACGTGCC TGAGCAGTCG GCTGTGACTC TCGACAATGT AACTCTGCAA 360
 45 ATCGATGGAG TCCTTTACCT GCGCATCATG GACCCTTACA AGGCAAGCTA CGGTGTGGAG 420
 GACCCTGAGT ATGCCGTCAC CCAGCTAGCT CAAACAACCA TGAGATCAGA GCTCGGCAAA 480
 50 CTCTCTCTGG ACAAAGTCTT CCGGAACGG GAGTCCCTGA ATGCCAGCAT TGTGGATGCC 540
 ATCAACCAAG CTGCTGACTG CTGGGGTATC CGCTGCCTCC GTTATGAGAT CAAGGATATC 600
 CATGTGCCAC CCCGGGTGAA AGAGTCTATG CAGATGCAGG TGGAGGCAGA GCGCGGAAA 660
 55 CGGGCCACAG TTCTAGAGTC TGAGGGGACC CGAGAGTCGG CCATCAATGT GGCAGAAGGG 720
 AAGAAACAGG CCCAGATCCT GGCCTCCGAA GCAGAAAAGG CTGAACAGAT AAATCAGGCA 780
 60 GCAGGAGAGG CCAGTGCACT TCTGGCGAAG GCCAAGGCTA AAGCTGAAGC TATTCGAATC 840

CTGGCTGCAG CTCTGACACA ACATAATGGA GATGCAGCAG CTTCACTGAC TGTGGCCGAG 900
CAGTATGTCA GCGCGTACTC CAAACTGGCC AAGGACTCCA ACACTATCCT ACTGCCCTCC 960
5 AACCCTGGCG ATGTCACCAG CATGGTGGCT CAGGCCATGG GTGTATATGG AGCCCTCACC 1020
AAAGCCCCAG TGCCAGGGAC TCCAGACTCA CTCTCCAGTG GGAGCAGCAG AGATGTCCAG 1080
10 GGTACAGATG CAAGTCTTGA TGAGGAACCT GATCGAGTCA AGATGAGTTA GTGGAGCTGG 1140
GCTTGGCCAG GGAGTCTGGG GACAAGGAAG CAGATTTTCC TGATTCTGGC TCTAGCTTCC 1200
CTGCCAAGAT TTGGTTTTTT ATTTTTTTAT TTGAACCTTA GTCGTGTAAT AAACCTACCA 1260
15 GTGGCAAACC AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 1320
NN 1322
20

(2) INFORMATION FOR SEQ ID NO: 103:

25 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 276 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
30 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 103:

NNATAGCTCA ACCATGTTCC AGGAGTGTAT TCCAATCAGC TTGTTTTTTC TTAAGTGGTT 60
35 AAAGGAATGT TGCTCAITTC CCTGCCCCAA CTCACATATT AACAAITGTT TAACTGGGAT 120
TAGATAAAAG GAAAGCTGAC TTACAGATGA ACCAAGAGGG AGCTATTTAT GCCACAGCCC 180
CCAGCCCACT AACTTTATGT TTCTGATCTC CTGCAAAATT TTTTATAAA AAAAGCTTAG 240
40 CCAGGAACCTA GTAGAAAGAA TAAAGTAAAG ATGGTG 276

45 (2) INFORMATION FOR SEQ ID NO: 104:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 381 base pairs
50 (B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 104:

55 GATTAAGGTA GAAAAGTACA GAAAACCTA AATTTTCATT GTGCTGTTTC AATGTGGCAG 60
ATTCCTTAAA ATACTTCGAC ACGCTACAAT AATTAAAGGT TTTAAGAACA TTAAGATACT 120
60 TAAAAAATAA AAGCCACAA TTGAATAACA AAAATGAACT TTGTTTTATT TTTTATTGGC 180

ATTAATGTAG GTTGCCGTGG TGAAAATAGT TTGAAATACT TCACAGTAAC AGTTTTTKTGC 240
 AGCCCTAGAG ATTAATAACA GCAAAGTAAA TAAGCAGGAC TCTCAACGAC TCATACTCAC 300
 5 AGACTGTTTA ATGIWATCCT ARCACTTCSG GARGCTGARG CGGGAGGATT ACTTGAGCCT 360
 AGGATTTGAG ACCAGCCTGG G 381

10

(2) INFORMATION FOR SEQ ID NO: 105:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 638 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 105:

TGTGGAAGAG AGTAGGAAAG CAATGAAAGA AGCTGGTAAG GGAGGCGTCG CTGATTCCAG 60
 25 AGAGCTAAAG CCGATGGTAG GTGGAGATGA RGARGTGCC GCCCTCCAAG AATTTCACCTT 120
 TCACTTCCTC TCTCTCTCTG TCTTCACTGA CTGCACTTCT TCAGGAGAAG CTTTGTGTAT 180
 CTGTATCAG CAGACATGCT GCTCTTCTG TTTGTGTGCT TACCCATCAC TTGGATGGCA 240
 30 GAATTCCTGT CAAACTGAG ACACCTYCTA TAAAAGTAAG CTGAAAGGAA CAGCATCCTC 300
 GTCAGTGCTC GGCAGGGGCG GGTAGGGGAT GATGGTTTTT TCCCTAAGGT AAAACTGCTG 360
 35 TTGCTCTGT TTTCTTTTAA ACTGTGAGT TTTGGCTTTC ATCAGACTGA ACAATTTGGT 420
 GTACACTTGA ACTGACGGTT TGATTTTTAT CATTTTGGAA GGTGATCATA GCAATTCCTT 480
 TCAACTTGCT AAAATTCATA CTCCTCTTT TAAAAGTATG GTTCTGCTTA CATTGCTGTC 540
 40 CTTTCCCTT GGCTGACTTT TTCTCTGTGT GCCTAGGTTG TACTTTTTTN TTTTTTTTNT 600
 TTTTCAGTAG CAAACAAGGC TGTTTTCATC AATACCCA 638

45

(2) INFORMATION FOR SEQ ID NO: 106:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 2246 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: double
 (D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 106:

GGCACGAGGC CGGGGAGAG TCACGCAAAT GACTTGGAGT GTTCAGGAAA AGGAAAATGC 60
 60 ACCACGAAGC CGTCAGAGGC AACTTTTTC TGTACCTGTG AGGAGCAGTA CGTGGGTACT 120

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|----|--|------|
| | TTCTGTGAAG AATACGATGC TTGCCAGAGG AAACCTTGCC AAAACAACGC GAGCTGTATT | 180 |
| 5 | GATGCAAATG AAAAGCAAGA TGGGAGCAAT TTCACCTGTG TTTGCCCTTC TGGTTATACT | 240 |
| | GGAGAGCTTT GCCAGTCCAA GATTGATTAC TGCATCCTAG ACCCATGCAG AAATGGAGCA | 300 |
| | ACATGCATTT CCAGTCTCAG TGGATTCAAC TGCCAGTGTG CAGAAGGATA CTTCCGATCT | 360 |
| 10 | GCTTGTGAAG AAAAGGTGGA CCCCTGCGCC TCGTCTCCGT GCCAGAACAA CGGCACCTGC | 420 |
| | TATGTGGACG GGGTACACTT TACCTGCAAC TGCAGCCCGG GCTTCACAGG GCCGACCTGT | 480 |
| 15 | GCCCAGCTTA TTGACTTCTG TGCCCTCAGC CCCTGTGCTC ATGGCACGTG CCGCAGCGTG | 540 |
| | GGCACCAGCT ACAAATGCCT CTGTGATCCA GGTACCATG GCCTCTACTG TGAGGAGGAA | 600 |
| | TATAATGAGT GECTCTCCGC TCCATGCCGT AATGCAGCCA CCTGCAGGGA CCTCGTTAAT | 660 |
| 20 | GGCTATGAGT GTGTGTGCCT GGCAGAATAC AAAGGAACAC ACTGTGAATT GTACAAGGAT | 720 |
| | CCCTGCGCTA ACGTCAGCTG TCTGAACGGA GCCACCTGTG ACAGCGACGG CCTGAATGGC | 780 |
| 25 | ACGTGCATCT GTGCACCCGG GTTTACAGGT GAAGAGTGCG ACATTGACAT AAATGAATGT | 840 |
| | GACAGTAACC CCTGCCACCA TGGTGGGAGC TGCCCTGACC AGCCCAATGG TTATAACTGC | 900 |
| | CACTGCCCGC ATGGTTGGGT GGGAGCAAAC TGTGAGATCC ACCTCCAATG GAAGTCCGGG | 960 |
| 30 | CACATGGCGG AGAGCCTCAC CAACATGCCA CGGCACTCCC TCTACATCAT CATGGAGGCC | 1020 |
| | CTCTGCGTGG CCTTCATCCT TATGCTGATC ATCCTGATCG TGGGGATTTG CCGCATCAGC | 1080 |
| 35 | CGCATTGAAT ACCAGGGTTC TTCCAGGCCA GCCTATGAGG AGTTCTACAA CTGCCGCAGC | 1140 |
| | ATCGACAGCG AGTTCAGCAA TGCCATTGCA TCCATCCGGC ATGCCAGGTT TGGAAAGAAA | 1200 |
| | TCCC CGCCTG CAATGTATGA TGTGAGCCCC ATCGCCTATG AAGATTACAG TCCTGATGAC | 1260 |
| 40 | AAACCTTGG TCACACTGAT TAAACTATAA GATTTGTAAT CTTTTTTTGG ATTATTTTTT | 1320 |
| | AAAAAGATGA GATACTACAC TCATTTAAAT ATTTTAAAG AAWTAAAAA GCTTAAGAAA | 1380 |
| 45 | TTTAAATGC TAGCTGCTCA AGRGTTTTCA GTAGAATATT TAAGAACTAA TTTTCTGCAG | 1440 |
| | CTTTTAGTTT GGAAAAAATA TTTTAAAAAC AAAATTGTG AAACCTATAG ACGATGTTTT | 1500 |
| | AATGTACCTT CAGCTCTCTA AACTGTGTGC TTCTACTAGT GTGTGCTCTT TTCCTGTAG | 1560 |
| 50 | ACACTATCAC GAGACCCAGA TTAATTTCTG TGGTTGTAC AGAATAAGTC TAATCAAGGA | 1620 |
| | GAAGTTTCTG TTTGACGTTT GAGTGCCGGC TTCTGAGTA GAGTTAGGAA AACCACGTAA | 1680 |
| 55 | CGTAGCATAT GATGTATAAT AGAGTATAAC CGTTACTTAA AAAGAAGTCT GAAATGTTTG | 1740 |
| | TTTTGTGGAA AAGAACTAG TTAATTTTAC TATTCCTAAC CCGAATGAAA TTAGCCTTTG | 1800 |
| | CCTTATTTCTG TGCATGGGTA AGTAACTTAT TTCTGCACTG TTTTGTGAA CTTTGTGGAA | 1860 |
| 60 | ACATTCCTTC GAGTTTGT TTGTCATTTT CGTAACAGTC GTCGAACTAG GCCTCAAAAA | 1920 |

5 CATACGTAAC GAAAAGGCCT AGCGAGGCAA ATTCIGATTG ATTTGAATCT ATATTTTCT 1980
TTAAAAAGTC AAGGGTTCTA TATGTGAGT AAATTAAATT TACATTGAG TTGTTTGTG 2040
CTAAGAGGTA GTAAATGTAA GAGAGTACTG GTTCCTTCAG TAGTGAGTAT TTCTCATAGT 2100
GCAGCTTTAT TTATCTCCAG GATGTTTTTG TGGCTGTATT TGATTGATAT GTGCTTCTTC 2160
10 TGATTCTTGC TAATTTCCTA CCATATTGAA TAAATGTGAT CAAGTCAAAA AAAAAAAAAA 2220
AAAAAAAAAT ACTCGGTCGC AAGGGA 2246

15

(2) INFORMATION FOR SEQ ID NO: 107:

20 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1105 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:

GAATTCGGCA GAGCCCACTT AGAGGAGCTA AAATAGCTAA AGGTTACATG CTTTGCCTCA 60
AATAATAGAC TTAGTGAAGA GGTAGAAGT AGAAATRAGG TCAGCCCCC AGAGCAGTCT 120
30 GGTGGCCTTR AGCAACCAGG AAGGTAAAGC CGGTACCTCA GTTAAATCAC CAAGTTTACT 180
GGAAGTGCAT ATTTTTCATG TGCCAAATTC AGTAAGTCAT GGAGCAAATG TTTATTTTGC 240
35 TATGCTTTAA AAAGTTGCTT GCTTCTTGTA AGTTTCTCA GTGGAAGGGT TCCAAGTTAT 300
GACTTAATCT ATGTTTGCAG CATGCACTG GAAACAGGAT TTGTCTGTGA AATGGCTCTG 360
TCATTGTGG ACCACTTCTG TAGGGAGATT GTGGATTTAG GAAGGCAGA AGCAACAGCA 420
40 GATATGCCTG GTGTTGAAT GGATGTGCTT CTYTCGGAGG CAGCAAGCAG CATACCCATA 480
TTATAAAGTT TTGATTTTC TAACATCTGA AGACAGGCAT CCAGCCTTGC AGAACAGCCA 540
45 GGTGCTGTT CTATAGACTA CAGTTCCTTG TTTCCAGAAT TACGGTAACC AAATAATACA 600
CAAGGTCACC TGATTGCACT TCCAACAAC CTGAACAAAG AGCACCTTTG CGCTTGCTGG 660
TAGGTGCTGT ACCAGACTCT TTGTAATCTG CCTTAGKTCA GRGAAGAACA AGCCATTACC 720
50 AGTATGGGAG TCCATCCYTA GTCAGGGCTA GTTGCTATTA TCCCTTGAAT ACTCTGCAGG 780
CATCCACAA GACATTTGAG ACTTCATATT TGTCAAATAA TAGAAATSTG GCTGGCCTAG 840
55 TGGCTCATGC CTGTAATCCT AACCCTTTGG GAGGCTGATG TGGGCAGATT GCTTGAGGCC 900
AGGAGTTTGA GACCCACCTG GGCAACACAG TGACATGTTG TCTCTACAAA AAATTTAAAA 960
ATTAAGTAGG CATGGTAGTG TGCCTATAGT CCCAGCTACT CCAGAGGCTG AGGCAGGAAG 1020
60

ATCCCTTGAG CCCAGTAAT CAAGGCTACA GTTAGCTCTG ATCCTGCCAC TGCACCTCTG 1080
TCTTGGTAAA GGAGCTAAAC CCACT 1105

5

(2) INFORMATION FOR SEQ ID NO: 108:

10

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 505 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108:

ATTTACACACA GGAAACAGCT ATGACCATGA TTCCGCCAAG CNCGAAATTA ACCNTCACTA 60
AAGGGAACAA AACTGGAGCT CCACCGCGGT GCGGCCGCT CTAGAACTAG TGGATCCCCC 120
GGGCTCAGGA ATTCGGCAGC AGTCTTCCA CATGTGTGCA CCCCAGCTT GGCCAACCTT 180
CAGCCTTGC GTGGGGCCG AAGCATCTTC CCTTCCGCTT GCGTCTCTG GGATTGGGAT 240
GAGTGCCTGG CTCCCATCTC CTCCTCACCT TTTGTTGCTA TCGGCAGCTG CTGGCTCAGG 300
GGCATCCAC CTCCGGGCTC TGGTTCTCTC TGCCCTGGAA GGGCTCCAGG ACCCGTCCCA 360
ATAACCACCC ACGCCAGGA GRGCCAAGGC CCCGTGCTGG ATATTTAAAT TTAGGGGCCG 420
GTCTCCAGGG CCGTAGATA AATAAATACA CTCAGCGTCA AAAAAAAAAA AAAAAAAAAA 480
AAAAAAAAA AAAAAAAAAA CTCGA 505

35

(2) INFORMATION FOR SEQ ID NO: 109:

40

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1380 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:

AATCATGAGC CTCCAGAAGA GACAGATGGC CCACCAGGAG CTGTTGCTCT GGTGCTTTC 60
CTGCAGCCT TGGAGAAGGA GGTGCCATA ATCGTTGACC AGAGAGCCTG GAACTTGCAC 120
CARAAGATTG TTGAAGATGC TGTGAGCAA GGTGTTCTGA AGACGCAGAT CCCGATATTA 180
ACTTACCAAG GTGGATCAGT GGAAGCTGCT CAGGCATTCC TGTGCAAAAA TGGGGACCCG 240
CAGACACCTA GATTGACCA CCTGGTGGCC ATAGAGCGTG CCGGAAGAGC TGCTGATGGC 300
AATTACTACA ATGCAAGGAA GATGAACATC AAGCACTTGG TTGACCCCAT TGACGATCTT 360

60

| | | |
|----|--|------|
| | TTTCTTGCTG CGAAGAAGAT TCCTGGAATC TCATCAACTG GAGTCGGTGA TGGAGGCAAC | 420 |
| | GAGCTTGGGA TGGGTAAAGT CAAGGAGGCT GTGAGGAGGC ACATACGGCA CGGGRATGTC | 480 |
| 5 | ATCGCCTGCG ACGTGGAGGC TGACTTTGCC GTCATTGCTG GTGTTTCTAA CTGGGGAGGC | 540 |
| | TATGCCCTGG CCTGCGCACT CTACATCCTG TACTCATGTG CTGTCCACAG TCAGTACCTG | 600 |
| 10 | AGGAAAGCAG TCGGACCCCTC CAGGGCACCT GGAGATCAGG CCTGGACTCA GGCCCTCCCG | 660 |
| | TCGGTCATTA AGGAAGAAAA AATGCTGGGC ATCTTGGTGC AGCACAAAGT CCGGAGTGGC | 720 |
| | GTCTCGGGCA TCGTGGGCAT GGAGGTGGAT GGGCTGCCCT TCCACAACAC CCACGCCGAG | 780 |
| 15 | ATGATCCAGA AGCTGGTGGG CGTCACCACG GCACAGGTGT AACCGTCCAT GTTCCGTGTG | 840 |
| | AGCAGAGTCC CTACCAACGG GCAGGTCTGC ATCCGGGGAG AATGCAGCTG CTTCTGGCGA | 900 |
| 20 | CAATCCTGCT AGTAAACACT GGTCTTCGGT GAGCAACGAA CACTCGCCTG GCCTGGGAAA | 960 |
| | CTGCATGCCC ACTTTCTGGG AGGGGTTAGT GCAGGTGCCG TGGACAAAGG ACAACATTTC | 1020 |
| | TCTGGGGCTT TTTAACTTTT ATTCTAAGA CTCTAAAGGC GTTGATTTC AACCCTCCTTC | 1080 |
| 25 | ACTCTGGCTT CTTCAGGCAA CCCACGTGGT CTCCTGTGAG AATCTTCTCG ACAGTTACTT | 1140 |
| | ATGGGGACAC TTGTGAACAA TTAAGTCCA GGCAGAGCAT GAGAACAAC ATTCCCAGGC | 1200 |
| 30 | CATGTAGGAT AGGATACTCC AGACTCCAGT CATCCTCCCC CATCCATGGT TTCTGTACT | 1260 |
| | CATGGTTTCA GTTACTCATA GCCAACTGCA GACCGAAAAT ACTAAATGAA AAATTTTCAGA | 1320 |
| 35 | AATAACAAC TCTTAAGTTT TAAAAAATA AAAAAAATA AAAAAAATA GGGCGGCCGC | 1380 |

(2) INFORMATION FOR SEQ ID NO: 110:

- 40 (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 646 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 110:

| | | |
|----|---|-----|
| | CAGATGCCAG GGACTTGGNC TTCCCCGGT TGAACCACAG GTTCCAAGAA ACCTGCAGGG | 60 |
| 50 | TCCAGCCTCC CCCCCATCCC CAGTYTTCCC CACCCTGGCC CGGCCCTCCA GGTGCAGAAA | 120 |
| | CATGCAGGCC CCTCTCCAGG ACTGTGGGAG GAGTGTGTCC CTCAGACTGG CTTGTGTCTT | 180 |
| 55 | GGCTCCTCTT ACCACCTCTT CCAGAGGTG TCACCTGCAG CTGCCCCAGG ATAAAGGCAA | 240 |
| | GGCCAGARAG GACTCCTGAA CTCCTGTGTG OCTGGGGTGG CAGGGGCAA CATAGCCAAC | 300 |
| | TGGTGGCCTG AGCGGGGCA TGGTGARGAC ACCCTTGGTG GCTTGTCCCA CATCAAGCTG | 360 |
| 60 | GGARGTGACA CTTAGGATGC ATTTTTCAT ATTTTGTGT TTGAATAACG GGCTAWCTTG | 420 |

AGAAAAAAT AATTTGAATC ACACATCACA CCAAAAATAA ATTCTAGGTG GATTTTAACA 480
 CTTTCCAAAA ATTATTATTA GTTTAGAGAC AGGGTCTCAC TCCGTCGCCT AGGCTGGAGT 540
 5 GCANGGGTAT GATCATGGTT CACTGCAACC TTAAACTCCC TGGCCTCATA TGATCCCCC 600
 GGGCTCCAGC CCCTCCAAAG TTACTGGGAA ACTACCAAAC ATGCCC 646
 10

(2) INFORMATION FOR SEQ ID NO: 111:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 32 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:
 20 Met Asp Ser Tyr Trp His Ser Arg Cys Leu Lys Cys Ser Cys Cys Gln
 1 5 10 15
 25 Ala Xaa Trp Ala Thr Ser Ala Arg Pro Val Thr Pro Lys Val Ala Xaa
 20 25 30

30

(2) INFORMATION FOR SEQ ID NO: 112:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 36 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:
 40 Ile Tyr Ser Ser Gly Tyr Phe Gln Ile Tyr Asn Met Leu Leu Leu Thr
 1 5 10 15
 Ile Leu Ile Leu Leu Cys Asn Arg Thr Pro Glu Leu Ile Pro Gly Phe
 20 25 30
 45 Tyr Ile Arg Xaa
 35

50

(2) INFORMATION FOR SEQ ID NO: 113:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 220 amino acids
 55 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:
 60 Met Ser His Lys Leu Gly Asp Pro Gly Phe Val Val Phe Ala Thr Leu
 1 5 10 15

265

Val Val Ile Val Ala Leu Ile Leu Ile Phe Val Val Gly Pro Arg His
 20 25 30

5 Gly Gln Thr Asn Ile Leu Val Tyr Ile Thr Ile Cys Ser Val Ile Gly
 35 40 45

Ala Phe Ser Val Ser Cys Val Lys Gly Leu Gly Ile Ala Ile Lys Glu
 50 55 60

10 Leu Phe Ala Gly Lys Pro Val Leu Arg His Pro Leu Ala Trp Ile Leu
 65 70 75 80

Leu Leu Ser Leu Ile Val Cys Val Ser Thr Gln Ile Asn Tyr Leu Asn
 85 90 95

15 Arg Ala Leu Asp Ile Phe Asn Thr Ser Ile Val Thr Pro Ile Tyr Tyr
 100 105 110

20 Val Phe Phe Thr Thr Ser Val Leu Thr Cys Ser Ala Ile Leu Phe Lys
 115 120 125

Glu Trp Gln Asp Met Pro Val Asp Asp Val Ile Gly Thr Leu Ser Gly
 130 135 140

25 Phe Phe Thr Ile Ile Val Gly Ile Phe Leu Leu His Ala Phe Lys Asp
 145 150 155 160

Val Ser Phe Ser Leu Ala Ser Leu Pro Val Ser Phe Arg Lys Asp Glu
 165 170 175

30 Lys Ala Met Asn Gly Asn Leu Ser Asn Met Tyr Glu Val Leu Asn Asn
 180 185 190

35 Asn Glu Glu Ser Leu Thr Cys Gly Ile Glu Gln His Thr Gly Glu Asn
 195 200 205

Val Ser Arg Arg Asn Gly Asn Leu Thr Ala Phe Xaa
 210 215 220

40

(2) INFORMATION FOR SEQ ID NO: 114:

- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 32 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:

50 Met Thr Ile Trp Glu Arg Lys Tyr Ile Trp Met Leu Gln Ile Cys Val
 1 5 10 15

Phe Leu Glu Pro Arg Ala Lys Pro Ser Leu Gly Asp Leu Asp Trp Xaa
 20 25 30

55

60

(2) INFORMATION FOR SEQ ID NO: 115:

- 5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 27 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:

10 Met Leu Thr Phe Leu Leu Phe Ile Pro Val Ala Pro Thr Glu Thr Ser
 1 5 10 15
 Gln Lys Asn Arg Ser Val Phe Leu Pro Pro Xaa
 20 25
 15

(2) INFORMATION FOR SEQ ID NO: 116:

- 20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 132 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:

25 Met Leu Phe Val Phe Cys Cys Thr Val Phe Phe Val Cys Leu Phe Val
 1 5 10 15
 Tyr Leu Val Gly Phe Leu Glu Arg Glu Ile Trp Lys Arg Asp Ile His
 20 25 30
 Lys Ser Tyr Thr Pro Thr Phe Pro Phe Tyr His Asp Ile Gln Glu Glu
 35 40 45
 35 Thr Ser Arg Ala Lys Asn Gly Val Lys Lys Gly Ser Met Ala Gly Thr
 50 55 60
 Ser Lys Glu Leu Arg Ala Val Ala Leu Lys Asn Tyr Phe Phe Tyr Tyr
 65 70 75 80
 40 Tyr Phe Glu Ser Met Glu Val Phe His Ser Leu Gly Lys Gly Gly Lys
 85 90 95
 Ser Ala Phe Ile Phe Ile Gln Ser Tyr Leu Ile Thr Ser Lys Thr His
 100 105 110
 45 Met Leu Glu Ile Ala Phe Ala Gly Ala Lys Tyr Ile Asn Glu Gln Glu
 115 120 125
 50 Tyr Ile His Xaa
 130

55 (2) INFORMATION FOR SEQ ID NO: 117:

- 60 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 65 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:

5 Met Trp Tyr Phe Met Ser Leu Ile Ser Met Val Leu Leu Leu Ser Pro
 1 5 10 15
 Ser Cys Ser Asp Leu Leu Val Ile Ser Val Leu Asn Leu Glu Gln Arg
 20 25 30
 10 Arg Gln Ser Lys Val Gly Phe Glu Pro Phe Thr Ser Pro Leu Cys Gly
 35 40 45
 Xaa Trp His His Leu Ser Pro Asp Arg Leu Pro Gln Asp Gly Thr Phe
 50 55 60
 15 Xaa
 65

20 (2) INFORMATION FOR SEQ ID NO: 118:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 9 amino acids
 (B) TYPE: amino acid
 25 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 118:

30 Leu Leu Leu Phe Cys Ile Leu Gly Xaa
 1 5

(2) INFORMATION FOR SEQ ID NO: 119:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 50 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:

40 Met Gly Val Leu Phe Val Pro Gln Glu Thr Ser Xaa Lys Val Xaa Xaa
 1 5 10 15
 45 Asp Ile Xaa Gly Leu Ser Gln Phe Val Met Gly Glu Lys Arg Thr Thr
 20 25 30
 Ser Ile Arg Gly Ile Gln Ala Arg Tyr Gln Val Asp Arg Gly Leu Glu
 35 40 45
 50 Tyr Cys
 50

55 (2) INFORMATION FOR SEQ ID NO: 120:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 76 amino acids
 (B) TYPE: amino acid
 60 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:

Met Leu Leu Leu Leu Leu Leu Leu Leu Leu Trp Thr Cys Gln
 1 5 10 15
 Lys Ala Leu Val Arg Arg Gln Phe Cys Leu Phe Asn Leu Ile Ala Arg
 20 25 30
 Asn Ser Ser Leu Met Leu Gln Lys Asp Glu Lys Lys Gly Lys Lys Arg
 35 40 45
 Asp Asn Ser Gln Ala Gln Arg Glu Lys Lys Gly Gly Gly Lys Glu Pro
 50 55 60
 Gln Gly Asp Leu Gln Glu Arg Pro Gly Pro Gly Xaa
 65 70 75

(2) INFORMATION FOR SEQ ID NO: 121:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:

Met His Asn Ala Phe Asn Leu Asn Val Leu Thr Leu Phe Leu Ser Val
 1 5 10 15
 Leu Cys Cys Thr Phe Ser Asp Ser Glu Leu Xaa
 20 25

(2) INFORMATION FOR SEQ ID NO: 122:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 122:

Met Ser Trp Leu Phe Leu Leu Phe Ala Leu Leu Cys Lys Phe Gln His
 1 5 10 15
 Lys Leu Xaa Phe His Asn Ile Xaa
 20

(2) INFORMATION FOR SEQ ID NO: 123:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:

Met Leu Leu Phe Leu Thr Val Ile Asn Phe Met Ala Leu Ala Lys Met

1 5 10 15

Asn Phe Cys Gly Asp Xaa
20

5

(2) INFORMATION FOR SEQ ID NO: 124:

10 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 55 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:

15

Met Val Xaa Asn Leu Gln Val Ile Ser Ile Trp Xaa Xaa Ser Thr Thr
1 5 10 15

20 Cys Phe Tyr Ala Cys Ile Trp Xaa Gln Gly Cys Leu Met Leu Arg Xaa
 20 25 30

Phe Xaa Thr Leu Asn Asn Val Thr Arg Leu Pro Ser Ser Gln Lys Pro
35 40 45

25 Ile Lys Cys Tyr Leu Leu Xaa
 50 55

30 (2) INFORMATION FOR SEQ ID NO: 125:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 318 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125:

Met Leu Ser Glu Ser Ser Ser Phe Leu Lys Gly Val Met Leu Gly Ser
1 5 10 15

40 Ile Phe Cys Ala Leu Ile Thr Met Leu Gly His Ile Arg Ile Gly His
 20 25 30

45 Gly Asn Arg Met His His His Glu His His His Leu Gln Ala Pro Asn
 35 40 45

Lys Glu Asp Ile Leu Lys Ile Ser Glu Asp Glu Arg Met Glu Leu Ser
50 55 60

50 Lys Ser Phe Arg Val Tyr Cys Ile Ile Leu Val Lys Pro Lys Asp Val
 65 70 75 80

Ser Leu Trp Ala Ala Val Lys Glu Thr Trp Thr Lys His Cys Asp Lys
85 90 95

55 Ala Glu Phe Phe Ser Ser Glu Asn Val Lys Val Phe Glu Ser Ile Asn
 100 105 110

60 Met Asp Thr Asn Asp Met Trp Leu Met Met Arg Lys Ala Tyr Lys Tyr
 115 120 125

270

Ala Phe Xaa Lys Thr Arg Asp Gln Tyr Asn Trp Phe Phe Leu Ala Arg
 130 135 140

5 Pro Thr Thr Phe Ala Ile Ile Glu Asn Leu Lys Tyr Phe Leu Leu Lys
 145 150 155 160

Lys Asp Pro Ser Gln Pro Phe Tyr Leu Gly His Thr Ile Lys Ser Gly
 165 170 175

10 Asp Leu Glu Tyr Val Gly Met Glu Gly Gly Ile Val Leu Ser Val Glu
 180 185 190

Ser Met Lys Arg Leu Asn Ser Leu Leu Asn Ile Pro Glu Lys Cys Pro
 195 200 205

15 Glu Gln Gly Gly Met Ile Trp Lys Ile Ser Glu Asp Lys Gln Leu Ala
 210 215 220

20 Val Cys Leu Lys Tyr Ala Gly Val Phe Ala Glu Asn Ala Glu Asp Ala
 225 230 235 240

Asp Gly Lys Asp Val Phe Asn Thr Lys Ser Val Gly Leu Ser Ile Lys
 245 250 255

25 Glu Ala Met Thr Tyr His Pro Asn Gln Val Val Glu Gly Cys Cys Ser
 260 265 270

30 Asp Met Ala Val Thr Phe Asn Gly Leu Thr Pro Asn Gln Met His Val
 275 280 285

Met Met Tyr Gly Val Tyr Arg Leu Arg Ala Phe Gly His Ile Phe Asn
 290 295 300

35 Asp Ala Leu Val Phe Leu Pro Pro Asn Gly Ser Asp Asn Asp
 305 310 315

40 (2) INFORMATION FOR SEQ ID NO: 126:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 59 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 126:

Met Thr Trp Pro Pro Ser Cys Leu Val Ala Leu Leu Leu Ser Thr Val
 1 5 10 15

50 Thr Gln Lys Met Thr Pro Leu Asn Leu Met Arg Thr Thr Gly Pro Ile
 20 25 30

Asn Ser Phe Cys Leu Leu Pro Thr Phe Phe Phe Phe Pro Ser Tyr Leu
 35 40 45

55 Pro Ser Leu Met Pro Thr Pro Thr Asp Pro Xaa
 50 55

60

(2) INFORMATION FOR SEQ ID NO: 127:

(i) SEQUENCE CHARACTERISTICS:

5

(A) LENGTH: 99 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127:

10 Ile Leu Phe Ser Phe Leu Ile Pro Ser Asn Leu Ser Phe Ser Pro Val
 1 5 10 15

Ile Phe Phe Leu Cys Gly Pro Phe Lys Val Val Ile Ile Cys Thr Glu
 20 25 30

15 Leu Gln Asn Val Ser Arg Ser Pro Gln Thr Thr Leu Ala Thr Val Tyr
 35 40 45

20 Cys Asn Lys Ile Thr Ser Tyr Ile Cys Arg Asn Ser Phe Gly Val Ile
 50 55 60

Leu Phe Phe Pro Leu Asn Ile Tyr Asn Trp Thr Asn Ala Gly Lys Lys
 65 70 75 80

25 Lys Lys Met Val Ser Lys Lys Pro Lys Ile Lys Phe Arg Gly His Gln
 85 90 95

Ala Phe Xaa

30

(2) INFORMATION FOR SEQ ID NO: 128:

(i) SEQUENCE CHARACTERISTICS:

35

(A) LENGTH: 29 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128:

40

Met Ser Ile Leu Leu Leu Xaa Phe Pro Ser Ala Pro Ala Pro Val Val
 1 5 10 15

Ser Gly Gly Leu Gln Pro Trp Leu His Ser Cys Ile Xaa
 20 25

45

(2) INFORMATION FOR SEQ ID NO: 129:

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129:

55

Met Gly Thr Ser Leu Asn Leu Gln Ile Met Ala Leu Phe Ser Gly Gln
 1 5 10 15

60

Ala Met Ala Pro Arg Xaa

5 (2) INFORMATION FOR SEQ ID NO: 130:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 112 amino acids

(B) TYPE: amino acid

10 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130:

Met Leu Trp Leu Pro Leu Leu Ala Ala Leu Ser Pro Ser Pro Gly
 1 5 10 15
 Val Ser Ser Glu Glu Glu Gln His Trp Ser Gln Ala Glu Ala Leu Pro
 20 25 30
 Cys Trp Asp Pro Gly Ser Glu Ser Ser Pro Arg Ile Pro Gly Cys Arg
 35 40 45
 Glu Leu Gln Ser Cys Pro Pro Pro Thr Ala Pro Ser Ala His Thr Gln
 50 55 60
 Ser Pro Gly Gly Leu Gly Ala Lys Ala Gly Ala Ala Leu Val Pro Phe
 65 70 75 80
 Pro Gly Pro Ser Phe Pro Thr Ser Lys Pro Lys Lys Gly Glu Ala Gly
 85 90 95
 Ala Pro Val Pro Gln Pro His Ser Ala Leu Thr Val Pro Ser Ser Xaa
 100 105 110

35

40 (2) INFORMATION FOR SEQ ID NO: 131:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 114 amino acids

(B) TYPE: amino acid

45 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

Met Glu Lys Pro Leu Phe Pro Leu Val Pro Leu His Trp Phe Gly Phe
 1 5 10 15
 Gly Tyr Thr Ala Leu Val Val Ser Gly Gly Ile Val Gly Tyr Val Lys
 20 25 30
 Thr Gly Ser Val Pro Ser Leu Ala Ala Gly Leu Leu Phe Gly Ser Leu
 35 40 45
 Ala Gly Leu Gly Ala Tyr Gln Leu Tyr Gln Asp Pro Arg Asn Val Trp
 50 55 60
 Gly Phe Leu Ala Ala Thr Ser Val Thr Phe Val Gly Val Met Gly Met
 65 70 75 80

Arg Ser Tyr Tyr Tyr Gly Lys Phe Met Pro Val Gly Leu Ile Ala Gly
85 90 95

5 Ala Ser Leu Leu Met Ala Ala Lys Val Gly Val Arg Met Leu Met Thr
100 105 110

Ser Asp

10

(2) INFORMATION FOR SEQ ID NO: 132:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:

20

Met Ile Thr Leu Leu Ile Trp Met Leu Ala Gly Phe Ile Ala Arg Ile
1 5 10 15

Xaa Val Ala Leu Gln Xaa
20

25

(2) INFORMATION FOR SEQ ID NO: 133:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 52 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 133:

Met Ala Gly Val Ser Glu Ile Ser Val Cys Phe Xaa Leu Leu Ser Leu
1 5 10 15

40

Phe Ser Leu Phe Cys Ser Phe Tyr Phe Pro Lys Gln Ala Thr Pro Lys
20 25 30

Arg Asp Leu Phe Val Gln Glu Ser Gly Lys Gly Lys Arg Asn Thr Glu
35 40 45

45

Ser Trp Glu Xaa
50

50

(2) INFORMATION FOR SEQ ID NO: 134:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 99 amino acids

55

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:

Met Thr Ser Ala Leu Thr Gln Gly Leu Glu Arg Ile Pro Asp Gln Leu
1 5 10 15

60

Gly Tyr Leu Val Leu Ser Glu Gly Ala Val Leu Ala Ser Ser Gly Asp
 20 25 30
 5 Leu Glu Asn Asp Glu Gln Ala Ala Ser Ala Ile Ser Glu Leu Val Ser
 35 40 45
 Thr Ala Cys Gly Phe Arg Leu His Arg Gly Met Asn Val Pro Phe Lys
 50 55 60
 10 Arg Leu Ser Val Val Phe Gly Glu His Thr Leu Leu Val Thr Val Ser
 65 70 75 80
 Gly Gln Arg Val Phe Val Val Lys Arg Gln Asn Arg Gly Arg Glu Pro
 15 85 90 95
 Ile Asp Val

20

(2) INFORMATION FOR SEQ ID NO: 135:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 176 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135:

30 Met Gly Ser Ala Ala Leu Glu Ile Leu Gly Leu Val Leu Cys Leu Val
 1 5 10 15
 Gly Trp Gly Gly Leu Ile Leu Ala Cys Gly Leu Pro Met Trp Gln Val
 20 25 30
 35 Thr Ala Phe Leu Asp His Asn Ile Val Thr Ala Gln Thr Thr Trp Lys
 35 40 45
 Gly Leu Trp Met Ser Cys Val Val Gln Ser Thr Gly His Met Gln Cys
 40 50 55 60
 Lys Val Tyr Asp Ser Val Leu Ala Leu Ser Thr Glu Val Gln Ala Ala
 65 70 75 80
 45 Arg Ala Leu Thr Val Ser Ala Val Leu Leu Ala Phe Val Ala Leu Phe
 85 90 95
 Val Thr Leu Ala Gly Ala Gln Cys Thr Thr Cys Val Ala Pro Gly Pro
 100 105 110
 50 Ala Lys Ala Arg Val Ala Leu Thr Gly Gly Val Leu Tyr Leu Phe Cys
 115 120 125
 Gly Leu Leu Ala Leu Val Pro Leu Cys Trp Phe Ala Asn Ile Val Val
 55 130 135 140
 Arg Glu Phe Tyr Asp Pro Ser Val Pro Val Ser Gln Lys Tyr Glu Leu
 145 150 155 160
 60 Gly Ala Xaa Cys Thr Ser Ala Gly Arg Pro Pro Arg Cys Ser Trp Xaa

165

170

175

5

(2) INFORMATION FOR SEQ ID NO: 136:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 187 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 136:

15

Met Val Leu Leu Trp Val Val Thr Cys Pro Ala Thr Met Leu Thr Glu
 1 5 10 15

20

Pro Gln Asn Pro His Leu Ile Gly Phe Val Ala Tyr Ser Gly Pro Ser
 20 25 30

His Thr Thr Gln Pro His Lys Tyr Trp Leu Leu Leu Asp Gly Gln Ala
 35 40 45

25

Asp Pro Ala Ala Ala Glu Gly Pro Val Lys Arg Lys Ala Ala Ser Val
 50 55 60

Val Trp Trp Pro Gln Ala Leu Arg His Leu Ser Leu Leu Val His Cys
 65 70 75 80

30

Trp Glu Glu Ser Tyr Glu Met Asn Ile Gly Cys Gln Ser Leu Trp Ala
 85 90 95

35

Gly Gly Leu Ala Ser Ser Gly Asn Gly Trp Asp Leu Gly Val Ala Phe
 100 105 110

Arg Arg Asp Thr Cys Met Ser Ser Ser Ser Leu His Trp Lys Glu Phe
 115 120 125

40

Lys Tyr Ala Pro Gly Ser Leu His Tyr Phe Ala Leu Ser Phe Val Leu
 130 135 140

Ile Leu Thr Glu Ile Cys Leu Val Ser Ser Gly Met Gly Phe Pro Gln
 145 150 155 160

45

Glu Gly Lys His Phe Ser Val Leu Gly Ser Pro Asp Cys Ser Leu Trp
 165 170 175

50

Gly Arg Asp Glu His Val Pro Arg Glu Phe Ala
 180 185

(2) INFORMATION FOR SEQ ID NO: 137:

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 288 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:

276

Met Pro Ala His Arg Phe Val Leu Ala Val Gly Ser Ala Val Phe Asn
 1 5 10 15
 5 Ala Met Phe Asn Gly Gly Met Ala Thr Thr Ser Thr Glu Ile Glu Leu
 20 25 30
 Pro Asp Val Glu Pro Ala Ala Phe Leu Ala Leu Leu Lys Phe Leu Tyr
 35 40 45
 10 Ser Asp Glu Val Gln Ile Gly Pro Glu Thr Val Met Thr Thr Xaa Tyr
 50 55 60
 Thr Ala Lys Lys Tyr Ala Val Pro Ala Leu Glu Ala His Cys Val Glu
 65 70 75 80
 Phe Leu Lys Lys Asn Leu Arg Ala Asp Asn Ala Phe Met Leu Leu Thr
 85 90 95
 20 Gln Ala Arg Leu Phe Asp Glu Pro Gln Leu Ala Ser Leu Cys Leu Glu
 100 105 110
 Asn Ile Asp Lys Asn Thr Ala Asp Ala Ile Thr Ala Glu Gly Phe Thr
 115 120 125
 25 Asp Ile Asp Leu Asp Thr Leu Val Ala Val Leu Glu Arg Asp Thr Leu
 130 135 140
 Gly Ile Arg Glu Val Arg Leu Phe Asn Ala Val Val Arg Trp Ser Glu
 145 150 155 160
 Ala Glu Cys Gln Arg Gln Gln Leu Gln Val Thr Pro Glu Asn Arg Arg
 165 170 175
 35 Lys Val Leu Gly Lys Ala Leu Gly Leu Ile Arg Phe Pro Leu Met Thr
 180 185 190
 Ile Glu Glu Phe Ala Ala Gly Pro Ala Gln Ser Gly Ile Leu Val Asp
 195 200 205
 40 Arg Glu Val Val Ser Leu Phe Cys Thr Ser Pro Ser Thr Pro Ser His
 210 215 220
 Glu Trp Ser Ser Leu Thr Gly Pro Ala Ala Ala Cys Val Gly Arg Ser
 225 230 235 240
 Ala Ala Ser Thr Ala Ser Ser Arg Trp Arg Val Ala Gly Ala Thr Xaa
 245 250 255
 50 Gly Pro Val Thr Ala Ser Gly Ser Gln Ser Thr Ser Ala Ser Ser Trp
 260 265 270
 Trp Asp Leu Gly Cys Met Asp Pro Ser Thr Gly Pro Pro Thr Thr Lys
 275 280 285
 55
 60

(2) INFORMATION FOR SEQ ID NO: 138:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 114 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 138:

5 Met Pro Arg Cys Arg Trp Leu Ser Leu Ile Leu Leu Thr Ile Pro Leu
 10 1 5 10 15
 Ala Leu Val Ala Arg Lys Asp Pro Lys Lys Asn Glu Thr Gly Val Leu
 20 25 30
 15 Arg Lys Leu Lys Pro Val Asn Ala Phe Xaa Cys Gln Arg Gly Ser Ser
 35 40 45
 Val Xaa Gly Phe Ala Met Gln Glu Tyr Asn Lys Glu Ser Glu Asp Lys
 50 55 60
 20 Tyr Val Phe Leu Val Val Lys Thr Leu Gln Ala Gln Leu Gln Val Thr
 65 70 75 80
 25 Asn Leu Leu Glu Tyr Leu Ile Asp Val Glu Ile Ala Arg Ser Asp Cys
 85 90 95
 Arg Lys Pro Leu Ser Thr Asn Glu Ile Ala Pro Phe Lys Xaa Thr Pro
 100 105 110
 30 Ser Xaa

35 (2) INFORMATION FOR SEQ ID NO: 139:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 120 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:

40 Met Ser Pro His Pro Thr Ala Leu Leu Gly Leu Val Leu Cys Leu Ala
 1 5 10 15
 45 Gln Thr Ile His Thr Gln Glu Glu Asp Leu Pro Arg Pro Ser Ile Ser
 20 25 30
 Ala Glu Pro Gly Thr Val Ile Pro Leu Gly Ser His Val Thr Phe Val
 50 35 40 45
 Cys Arg Gly Pro Val Gly Val Gln Thr Phe Arg Leu Glu Arg Glu Ser
 50 55 60
 55 Arg Ser Thr Tyr Asn Asp Thr Glu Asp Val Ser Gln Ala Ser Pro Ser
 65 70 75 80
 Glu Ser Glu Ala Arg Phe Arg Ile Asp Ser Val Ser Glu Gly Asn Ala
 85 90 95
 60

Gly Pro Tyr Arg Cys Ile Tyr Tyr Lys Pro Pro Lys Trp Ser Glu Gln
 100 105 110

5 Ser Asp Tyr Trp Ser Cys Trp Xaa
 115 120

(2) INFORMATION FOR SEQ ID NO: 140:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 438 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 140:

Met Asn Thr Pro Asn Gly Asn Ser Leu Ser Ala Ala Glu Leu Thr Cys
 1 5 10 15

20 Gly Met Ile Met Cys Leu Ala Arg Gln Ile Pro Gln Ala Thr Ala Ser
 20 25 30

Met Lys Asp Gly Lys Trp Glu Arg Lys Lys Phe Met Gly Thr Glu Leu
 35 40 45

25

Asn Gly Lys Thr Leu Gly Ile Leu Gly Leu Gly Arg Ile Gly Arg Glu
 50 55 60

30 Val Ala Thr Arg Met Gln Ser Phe Gly Met Lys Thr Ile Gly Tyr Asp
 65 70 75 80

Pro Ile Ile Ser Pro Glu Val Ser Ala Ser Phe Gly Val Gln Gln Leu
 85 90 95

35 Pro Leu Glu Glu Ile Trp Pro Leu Cys Asp Phe Ile Thr Val His Thr
 100 105 110

Pro Leu Leu Pro Ser Thr Thr Gly Leu Leu Asn Asp Asn Thr Phe Ala
 115 120 125

40

Gln Cys Lys Lys Gly Val Arg Val Val Asn Cys Ala Arg Gly Gly Ile
 130 135 140

45 Val Asp Glu Gly Ala Leu Leu Arg Ala Leu Gln Ser Gly Gln Cys Ala
 145 150 155 160

Gly Ala Ala Leu Asp Val Phe Thr Glu Glu Pro Pro Arg Asp Arg Ala
 165 170 175

50 Leu Val Asp His Glu Asn Val Ile Ser Cys Pro His Leu Gly Ala Ser
 180 185 190

Thr Lys Glu Ala Gln Ser Arg Cys Gly Glu Glu Ile Ala Val Gln Phe
 195 200 205

55

Val Asp Met Val Lys Gly Lys Ser Leu Thr Gly Val Val Asn Ala Gln
 210 215 220

60 Ala Leu Thr Ser Ala Phe Ser Pro His Thr Lys Pro Trp Ile Gly Leu
 225 230 235 240

279

Ala Glu Ala Leu Gly Thr Leu Met Arg Ala Trp Ala Gly Ser Pro Lys
 245 250 255

5 Gly Thr Ile Gln Val Ile Thr Gln Gly Thr Ser Leu Lys Asn Ala Gly
 260 265 270

Asn Cys Leu Ser Pro Ala Val Ile Val Gly Leu Leu Lys Glu Ala Ser
 275 280 285

10 Lys Gln Ala Asp Val Asn Leu Val Asn Ala Lys Leu Leu Val Lys Glu
 290 295 300

Ala Gly Leu Asn Val Thr Thr Ser His Ser Pro Ala Ala Pro Gly Glu
 305 310 315 320

Gln Gly Phe Gly Glu Cys Leu Leu Ala Val Ala Leu Ala Gly Ala Pro
 325 330 335

20 Tyr Gln Ala Val Gly Leu Val Gln Gly Thr Thr Pro Val Leu Gln Gly
 340 345 350

Leu Asn Gly Ala Val Phe Arg Pro Glu Val Pro Leu Arg Arg Asp Leu
 355 360 365

25 Pro Leu Leu Leu Phe Arg Thr Gln Thr Ser Asp Pro Ala Met Leu Pro
 370 375 380

Thr Met Ile Gly Leu Leu Ala Glu Ala Gly Val Arg Leu Leu Ser Tyr
 385 390 395 400

Gln Thr Ser Leu Val Ser Asp Gly Glu Thr Trp His Val Met Gly Ile
 405 410 415

35 Ser Ser Leu Leu Pro Ser Leu Glu Ala Trp Lys Gln His Val Thr Glu
 420 425 430

Ala Phe Gln Phe His Phe
 435

40

(2) INFORMATION FOR SEQ ID NO: 141:

- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 164 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

50 Met Ser Arg Pro Thr His Thr Pro Leu Ser Pro Ala Thr Ile Ser Pro
 1 5 10 15

Thr Ile Thr Val Ala Val Phe Phe Ala Val Phe Val Ala Ala Ala Ala
 20 25 30

55 Ala Thr Ala Val Val Ala Val Ala Ala Ala Thr Thr Ser Ser Gly Arg
 35 40 45

60 Arg Thr Xaa Asp Lys Ser Pro Ile Ala Thr Gln Ser Ser Val Thr His

280

50 55 60

Ile Ala Ala Lys Arg Cys His Asn Tyr Thr Glu Cys Leu Ser Leu Ile
65 70 75 80

5 Arg Xaa Thr Arg Ile Pro Thr Trp Xaa Xaa Xaa Thr Thr Cys Pro Ser
 85 90 95

10 Arg Ile Pro Ser Thr His Val Ala Ala Gly Ala Gly Phe Ile Arg Glu
 100 105 110

Arg Ala Cys Leu Gln Cys Gly Ala Val Gly Pro Pro Gly Cys Ile Leu
115 120 125

15 Ala Ser Leu Pro Pro Pro Ser Leu Tyr Leu Ser Pro Glu Leu Arg Cys
130 135 140

Met Pro Lys Arg Val Glu Ala Arg Ser Glu Leu Arg Leu Cys Pro Pro
145 150 155 160

20 Gly Val Xaa Xaa

25

(2) INFORMATION FOR SEQ ID NO: 142:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 73 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 142:

35 Met Gln Arg Trp Val Cys Ile Leu Glu Phe Lys Glu Asn Leu Phe Gln
1 5 10 15

Ile Pro Ser Ser Leu Val Ala Leu Leu Asn Thr Leu Phe Leu Asp Ile
20 25 30

40 Leu His Pro Gln Asn Ser Leu Ser Pro His Gly Ser Phe Ser Leu Ser
35 40 45

Ser Leu Ser Phe Pro Pro Leu Pro Val Ser Ser Leu Gln Pro Phe Leu
50 55 60

45 Phe Leu Arg Ser Leu Leu Cys Arg Xaa
65 70

50

(2) INFORMATION FOR SEQ ID NO: 143:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 123 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 143:

60 Phe Gly Thr Arg Phe Leu Ala Asn Leu Leu Leu Glu Glu Asp Asn Lys
1 5 10 15

Phe Cys Ala Asp Cys Gln Ser Lys Gly Pro Arg Trp Ala Ser Trp Asn
 20 25 30

5 Ile Gly Val Phe Ile Cys Ile Arg Cys Ala Xaa Ile His Arg Asn Leu
 35 40 45

Gly Val His Ile Ser Arg Val Lys Ser Val Asn Leu Asp Gln Trp Thr
 50 55 60

10 Gln Val Gln Ile Gln Cys Met Gln Xaa Met Gly Asn Gly Lys Ala Asn
 65 70 75 80

15 Arg Leu Tyr Glu Ala Tyr Leu Pro Glu Thr Phe Arg Arg Pro Gln Ile
 85 90 95

Asp Pro Ala Val Glu Gly Phe Ile Arg Asp Xaa Tyr Glu Lys Lys Lys
 100 105 110

20 Tyr Met Asp Arg Ser Leu Gly His Gln Cys Leu
 115 120

25 (2) INFORMATION FOR SEQ ID NO: 144:

 (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 138 amino acids

 (B) TYPE: amino acid

 (D) TOPOLOGY: linear

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 144:

Met Ser Leu Tyr Asp Asp Leu Gly Val Glu Thr Ser Asp Ser Lys Thr
 1 5 10 15

35 Glu Gly Trp Ser Lys Asn Phe Lys Leu Leu Gln Ser Gln Leu Gln Val
 20 25 30

40 Lys Lys Ala Ala Leu Thr Gln Ala Lys Ser Gln Arg Thr Lys Gln Ser
 35 40 45

Thr Val Leu Ala Pro Val Ile Asp Leu Lys Arg Gly Gly Ser Ser Asp
 50 55 60

45 Asp Arg Gln Ile Val Asp Thr Pro Pro His Val Ala Ala Gly Leu Lys
 65 70 75 80

50 Asp Pro Val Pro Ser Gly Phe Ser Ala Gly Glu Val Leu Ile Pro Leu
 85 90 95

Ala Asp Glu Tyr Asp Pro Met Phe Pro Asn Asp Tyr Glu Lys Val Val
 100 105 110

55 Lys Arg Ala Lys Arg Gly Thr Thr Glu Thr Ala Gly Val Xaa Lys Thr
 115 120 125

Lys Gly Asn Arg Arg Lys Gly Lys Lys Ala
 130 135

60

(2) INFORMATION FOR SEQ ID NO: 145:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 356 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 356 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

10 Met Leu Ala Arg Ala Ala Arg Gly Thr Gly Ala Leu Leu Leu Arg Gly
 1 5 10 15
 Ser Leu Leu Ala Ser Gly Arg Ala Pro Arg Arg Ala Ser Ser Gly Leu
 20 25 30
 15 Pro Arg Asn Thr Val Val Leu Phe Val Pro Gln Gln Glu Ala Trp Val
 35 40 45
 Val Glu Arg Met Gly Arg Phe His Arg Ile Leu Glu Pro Gly Leu Asn
 20 50 55 60
 Ile Leu Ile Pro Val Leu Asp Arg Ile Arg Tyr Val Gln Ser Leu Lys
 65 70 75 80
 25 Glu Ile Val Ile Asn Val Pro Glu Gln Ser Ala Val Thr Leu Asp Asn
 85 90 95
 Val Thr Leu Gln Ile Asp Gly Val Leu Tyr Leu Arg Ile Met Asp Pro
 100 105 110
 30 Tyr Lys Ala Ser Tyr Gly Val Glu Asp Pro Glu Tyr Ala Val Thr Gln
 115 120 125
 Leu Ala Gln Thr Thr Met Arg Ser Glu Leu Gly Lys Leu Ser Leu Asp
 35 130 135 140
 Lys Val Phe Arg Glu Arg Glu Ser Leu Asn Ala Ser Ile Val Asp Ala
 145 150 155 160
 40 Ile Asn Gln Ala Ala Asp Cys Trp Gly Ile Arg Cys Leu Arg Tyr Glu
 165 170 175
 Ile Lys Asp Ile His Val Pro Pro Arg Val Lys Glu Ser Met Gln Met
 180 185 190
 45 Gln Val Glu Ala Glu Arg Arg Lys Arg Ala Thr Val Leu Glu Ser Glu
 195 200 205
 Gly Thr Arg Glu Ser Ala Ile Asn Val Ala Glu Gly Lys Lys Gln Ala
 50 210 215 220
 Gln Ile Leu Ala Ser Glu Ala Glu Lys Ala Glu Gln Ile Asn Gln Ala
 225 230 235 240
 55 Ala Gly Glu Ala Ser Ala Val Leu Ala Lys Ala Lys Ala Lys Ala Glu
 245 250 255
 Ala Ile Arg Ile Leu Ala Ala Ala Leu Thr Gln His Asn Gly Asp Ala
 260 265 270
 60

283

Ala Ala Ser Leu Thr Val Ala Glu Gln Tyr Val Ser Ala Phe Ser Lys
 275 280 285

5 Leu Ala Lys Asp Ser Asn Thr Ile Leu Leu Pro Ser Asn Pro Gly Asp
 290 295 300

Val Thr Ser Met Val Ala Gln Ala Met Gly Val Tyr Gly Ala Leu Thr
 305 310 315 320

10 Lys Ala Pro Val Pro Gly Thr Pro Asp Ser Leu Ser Ser Gly Ser Ser
 325 330 335

Arg Asp Val Gln Gly Thr Asp Ala Ser Leu Asp Glu Glu Leu Asp Arg
 340 345 350

15 Val Lys Met Ser
 355

20

(2) INFORMATION FOR SEQ ID NO: 146:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 40 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 146:

30 Met Tyr Ile Leu Leu Phe Trp Gly Gly Xaa Phe His Arg Cys Leu Ser
 1 5 10 15

Xaa Leu Phe Asp Pro Glu Leu Xaa Ser Xaa Pro Gly Ile Ser Xaa Phe
 20 25 30

35 Thr Val Xaa Leu Gln Met Thr Xaa
 35 40

40

(2) INFORMATION FOR SEQ ID NO: 147:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 71 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 147:

Met Pro Ser Pro Lys Tyr Cys Met His Thr Asn Asp Val Gln Ser Val
 1 5 10 15

50 Glu Tyr Asn Gly Asp Thr Leu Phe Gln Lys Leu Ser Ser Ser Xaa Leu
 20 25 30

Ser Phe Lys Ser Ile His Ile Tyr Pro Asn Glu Xaa Lys Thr Cys Xaa
 35 40 45

55 Xaa Ile Phe Ile Ser Lys Val Tyr Met Ile Ser Lys Thr Trp Lys Xaa
 50 55 60

60 Pro Arg Phe Thr Ser Xaa Gly

65

70

5 (2) INFORMATION FOR SEQ ID NO: 148:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 148:

Met Asn Phe Val Leu Phe Phe Ile Gly Ile Asn Val Gly Cys Arg Gly
 1 5 10 15

15

Glu Asn Ser Leu Lys Tyr Phe Thr Val Thr Val Leu Cys Ser Pro Arg
 20 25 30

Asp

20

25 (2) INFORMATION FOR SEQ ID NO: 149:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 78 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 149:

Met Lys Glu Ala Gly Lys Gly Gly Val Ala Asp Ser Arg Glu Leu Lys
 1 5 10 15

35

Pro Met Val Gly Gly Asp Glu Glu Val Ala Ala Leu Gln Glu Phe His
 20 25 30

Phe His Phe Leu Ser Leu Ser Val Phe Thr Asp Cys Thr Ser Ser Gly
 35 40 45

40

Glu Ala Phe Val Ile Cys Ile Thr Gln Thr Cys Cys Ser Phe Cys Leu
 50 55 60

Cys Ala Tyr Pro Ser Leu Gly Trp Gln Asn Ser Cys His Asn
 65 70 75

45

50 (2) INFORMATION FOR SEQ ID NO: 150:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 150:

Met Phe Ser Ser Lys Ser Leu Leu Val Leu Pro Phe Cys Phe Arg Ser
 1 5 10 15

60

Ala Ala His Leu Glu Leu Ser Val Trp Cys Val Cys Gly Val Arg Xaa

20

25

30

5

(2) INFORMATION FOR SEQ ID NO: 151:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 464 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 151:

15

Met Leu Ala Leu Gly Asn Asn His Phe Ile Gly Phe Val Asn Asp Ser
 1 5 10 15

20

Val Thr Lys Ser Ile Val Ala Leu Arg Leu Thr Leu Val Val Lys Val
 20 25 30

Ser Thr Xaa Pro Gly Glu Ser His Ala Asn Asp Leu Glu Cys Ser Gly
 35 40 45

25

Lys Gly Lys Cys Thr Thr Lys Pro Ser Glu Ala Thr Phe Ser Cys Thr
 50 55 60

Cys Glu Glu Gln Tyr Val Gly Thr Phe Cys Glu Glu Tyr Asp Ala Cys
 65 70 75 80

30

Gln Arg Lys Pro Cys Gln Asn Asn Ala Ser Cys Ile Asp Ala Asn Glu
 85 90 95

35

Lys Gln Asp Gly Ser Asn Phe Thr Cys Val Cys Leu Pro Gly Tyr Thr
 100 105 110

Gly Glu Leu Cys Gln Ser Lys Ile Asp Tyr Cys Ile Leu Asp Pro Cys
 115 120 125

40

Arg Asn Gly Ala Thr Cys Ile Ser Ser Leu Ser Gly Phe Thr Cys Gln
 130 135 140

Cys Pro Glu Gly Tyr Phe Gly Ser Ala Cys Glu Glu Lys Val Asp Pro
 145 150 155 160

45

Cys Ala Ser Ser Pro Cys Gln Asn Asn Gly Thr Cys Tyr Val Asp Gly
 165 170 175

50

Val His Phe Thr Cys Asn Cys Ser Pro Gly Phe Thr Gly Pro Thr Cys
 180 185 190

Ala Gln Leu Ile Asp Phe Cys Ala Leu Ser Pro Cys Ala His Gly Thr
 195 200 205

55

Cys Arg Ser Val Gly Thr Ser Tyr Lys Cys Leu Cys Asp Pro Gly Tyr
 210 215 220

His Gly Leu Tyr Cys Glu Glu Glu Tyr Asn Glu Cys Leu Ser Ala Pro
 225 230 235 240

60

286

Cys Leu Asn Ala Ala Thr Cys Arg Asp Leu Val Asn Gly Tyr Glu Cys
 245 250 255
 5 Val Cys Leu Ala Glu Tyr Lys Gly Thr His Cys Glu Leu Tyr Lys Asp
 260 265 270
 Pro Cys Ala Asn Val Ser Cys Leu Asn Gly Ala Thr Cys Asp Ser Asp
 275 280 285
 10 Gly Leu Asn Gly Thr Cys Ile Cys Ala Pro Gly Phe Thr Gly Glu Glu
 290 295 300
 Cys Asp Ile Asp Ile Asn Glu Cys Asp Ser Asn Pro Cys His His Gly
 305 310 315 320
 15 Gly Ser Cys Leu Asp Gln Pro Asn Gly Tyr Asn Xaa His Cys Pro His
 325 330 335
 Gly Trp Val Gly Ala Asn Cys Glu Ile His Leu Gln Trp Lys Ser Gly
 340 345 350
 20 His Met Ala Glu Ser Leu Thr Asn Met Pro Arg His Ser Leu Tyr Ile
 355 360 365
 25 Ile Ile Gly Ala Leu Cys Val Ala Phe Ile Leu Met Leu Ile Ile Leu
 370 375 380
 Ile Val Gly Ile Cys Arg Ile Ser Arg Ile Glu Tyr Gln Gly Ser Ser
 385 390 395 400
 30 Arg Pro Ala Tyr Xaa Glu Phe Tyr Asn Cys Arg Ser Ile Asp Ser Glu
 405 410 415
 Phe Ser Asn Ala Ile Ala Ser Ile Arg His Ala Arg Phe Gly Lys Lys
 420 425 430
 35 Ser Arg Pro Ala Met Tyr Asp Val Ser Pro Ile Ala Tyr Glu Asp Tyr
 435 440 445
 40 Ser Pro Asp Asp Lys Pro Leu Val Thr Leu Ile Lys Thr Lys Asp Leu
 450 455 460

45

(2) INFORMATION FOR SEQ ID NO: 152:

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 151 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 152:

55

Met His His Gln Met Thr Arg Thr Thr Leu Met Thr Lys Gln His Glu
 1 5 10 15

60

Leu Gly Gly Leu Leu Ala Leu Val Gln Asn Cys Gln Ser Glu Met Asn
 20 25 30

Ile Lys Asp Ser Arg Ala Val Gly Leu Ser Val Lys Arg Leu Cys Ile
 35 40 45

5 Ser Phe Val Asp Glu Phe Cys Glu Arg Thr Glu Arg Pro Leu Tyr Leu
 50 55 60

Ala Gln Gly Leu Phe Met Lys Arg Glu Thr Tyr Trp Glu Val Gln Asp
 65 70 75 80

10 Ser Gly Ile Ser Pro Leu Leu Leu Leu Ser Thr Ala Leu Asp Cys
 85 90 95

Ser Pro Glu Ala Glu Thr Arg Gln Ser Pro Gly Gly Arg Lys Met Leu
 100 105 110

Gln Glu Pro Thr Leu Ser Met Ser Leu Gln Ile Leu Thr Gly Phe Leu
 115 120 125

20 Trp Val Gln Leu Trp Asn Trp Glu Thr Phe Leu Arg Ile Arg Thr His
 130 135 140

Ser Thr Asp Ala Ser Cys Pro
 145 150

25

(2) INFORMATION FOR SEQ ID NO: 153:

30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 299 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:

35 Met Ala Gln Asn Leu Lys Asp Leu Ala Gly Arg Leu Pro Ala Gly Pro
 1 5 10 15

Arg Gly Met Gly Thr Ala Leu Lys Leu Leu Leu Gly Ala Gly Ala Val
 20 25 30

Ala Tyr Gly Val Arg Glu Ser Val Phe Thr Val Glu Gly Gly His Arg
 35 40 45

45 Ala Ile Phe Phe Asn Arg Ile Gly Gly Val Gln Gln Asp Thr Ile Leu
 50 55 60

Ala Glu Gly Leu His Phe Arg Ile Pro Trp Phe Gln Tyr Pro Ile Ile
 65 70 75 80

50 Tyr Asp Ile Arg Ala Arg Pro Arg Lys Ile Ser Ser Pro Thr Gly Ser
 85 90 95

Lys Asp Leu Gln Met Val Asn Ile Ser Leu Arg Val Leu Ser Arg Pro
 100 105 110

Asn Ala Gln Glu Leu Pro Ser Met Tyr Gln Arg Leu Gly Leu Asp Tyr
 115 120 125

60 Glu Glu Arg Val Leu Pro Ser Ile Val Asn Glu Val Leu Lys Ser Val

288

130 135 140
 Val Ala Lys Phe Asn Ala Ser Gln Leu Ile Thr Gln Arg Ala Gln Val
 145 150 155 160
 5 Ser Leu Leu Ile Arg Arg Glu Leu Thr Glu Arg Ala Lys Asp Phe Ser
 165 170 175
 Leu Ile Leu Asp Asp Val Ala Ile Thr Glu Leu Ser Phe Ser Arg Glu
 10 180 185 190
 Tyr Thr Ala Ala Val Glu Ala Lys Gln Val Ala Gln Gln Glu Ala Gln
 195 200 205
 15 Arg Ala Xaa Phe Leu Val Glu Lys Ala Lys Gln Glu Gln Arg Gln Lys
 210 215 220
 Ile Val Gln Ala Glu Gly Glu Ala Glu Ala Ala Lys Met Leu Gly Glu
 20 225 230 235 240
 Ala Leu Ser Lys Asn Pro Gly Tyr Ile Lys Leu Arg Lys Ile Arg Ala
 245 250 255
 25 Ala Gln Asn Ile Ser Lys Thr Ile Ala Thr Ser Gln Asn Arg Ile Tyr
 260 265 270
 Leu Thr Ala Asp Asn Leu Val Leu Asn Leu Gln Asp Glu Ser Phe Thr
 275 280 285
 30 Arg Gly Ser Asp Ser Leu Ile Lys Gly Lys Lys
 290 295

35 (2) INFORMATION FOR SEQ ID NO: 154:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 398 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 154:

Met Leu Arg Gly Pro Trp Arg Gln Leu Trp Leu Phe Xaa Leu Leu Leu
 1 5 10 15
 45 Leu Pro Gly Ala Pro Glu Pro Arg Gly Ala Ser Arg Pro Trp Glu Gly
 20 25 30
 Thr Asp Glu Pro Gly Ser Ala Trp Ala Trp Pro Gly Phe Gln Arg Leu
 50 35 40 45
 Gln Glu Gln Leu Arg Ala Ala Gly Ala Leu Ser Lys Arg Tyr Trp Thr
 50 55 60
 55 Leu Phe Ser Cys Gln Val Trp Pro Asp Asp Cys Asp Glu Asp Glu Glu
 65 70 75 80
 Ala Ala Thr Gly Pro Leu Gly Trp Arg Leu Pro Leu Leu Gly Gln Arg
 85 90 95
 60

289

Tyr Leu Asp Leu Leu Thr Thr Trp Tyr Cys Ser Phe Lys Asp Cys Cys
 100 105 110

5 Pro Arg Gly Asp Cys Arg Ile Ser Asn Asn Phe Thr Gly Leu Glu Trp
 115 120 125

Asp Leu Asn Val Arg Leu His Gly Gln His Leu Val Gln Gln Leu Val
 130 135 140

10 Leu Arg Thr Val Arg Gly Tyr Leu Glu Thr Pro Gln Pro Glu Lys Ala
 145 150 155 160

Leu Ala Leu Ser Phe His Gly Trp Ser Gly Thr Gly Lys Asn Phe Val
 165 170 175

15 Ala Arg Met Leu Val Glu Asn Leu Tyr Arg Asp Gly Leu Met Ser Asp
 180 185 190

20 Cys Val Arg Met Phe Ile Ala Thr Phe His Phe Pro His Pro Lys Tyr
 195 200 205

Val Asp Leu Tyr Lys Glu Gln Leu Met Ser Gln Ile Arg Glu Thr Gln
 210 215 220

25 Gln Leu Cys His Gln Thr Leu Phe Ile Phe Asp Glu Ala Glu Lys Leu
 225 230 235 240

His Pro Gly Leu Leu Glu Val Leu Gly Pro His Leu Glu Arg Arg Ala
 245 250 255

30 Pro Xaa Gly His Arg Ala Glu Ser Pro Trp Thr Ile Phe Leu Phe Leu
 260 265 270

35 Ser Asn Leu Arg Gly Asp Ile Ile Asn Glu Val Val Leu Lys Leu Leu
 275 280 285

Lys Ala Gly Trp Ser Arg Glu Glu Ile Thr Met Glu His Leu Glu Pro
 290 295 300

40 His Leu Gln Ala Glu Ile Val Glu Thr Ile Asp Asn Gly Phe Gly His
 305 310 315 320

Ser Arg Leu Val Lys Glu Asn Leu Ile Asp Tyr Phe Ile Pro Phe Leu
 325 330 335

45 Pro Leu Glu Tyr Arg His Val Arg Leu Cys Ala Arg Asp Ala Phe Leu
 340 345 350

50 Ser Gln Glu Leu Leu Tyr Lys Glu Glu Thr Leu Asp Glu Ile Ala Gln
 355 360 365

Met Met Val Tyr Val Pro Lys Glu Glu Gln Leu Phe Ser Ser Gln Gly
 370 375 380

55 Cys Lys Ser Ile Ser Gln Arg Ile Asn Tyr Phe Leu Ser Xaa
 385 390 395

60 (2) INFORMATION FOR SEQ ID NO: 155:
 --

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 83 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 155:

5 Met Ala Phe Thr Leu Tyr Ser Leu Leu Gln Ala Xaa Leu Leu Cys Val
 1 5 10 15
 10 Asn Ala Ile Ala Val Leu His Glu Glu Arg Phe Leu Lys Asn Ile Gly
 20 25 30
 15 Trp Gly Thr Asp Gln Gly Ile Gly Gly Phe Gly Glu Glu Pro Gly Ile
 35 40 45
 Lys Ser Gln Leu Met Asn Leu Ile Arg Ser Val Arg Thr Val Met Arg
 50 55 60
 20 Val Pro Leu Ile Ile Val Asn Ser Ile Ala Ile Val Leu Leu Leu Leu
 65 70 75 80
 Phe Gly Xaa

25

(2) INFORMATION FOR SEQ ID NO: 156:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 50 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 156:

35

35 Met Ala Pro Arg Asn Gln Gly Ser Phe Ser Phe Gly Asn Phe Met Leu
 1 5 10 15
 40 Phe Leu Val Leu Ile Glu Arg Arg Tyr Leu Pro Phe Leu Ser Pro Ile
 20 25 30
 Leu Phe Cys Cys Ser Thr His Asn Arg Ser Ala Val Thr Ala Thr Asn
 35 40 45
 45 Leu Xaa
 50

50

(2) INFORMATION FOR SEQ ID NO: 157:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 51 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:

55

55 Met Asp Val Leu Thr Val Ala Phe Leu Ser Ile Leu Ile Thr Ala Pro
 1 5 10 15
 60

Ile Gly Ser Leu Leu Ile Gly Leu Leu Gly Pro Arg Leu Leu Gln Lys
 20 25 30
 5 Val Glu His Gln Asn Lys Asp Glu Glu Val Gln Gly Glu Thr Ser Val
 35 40 45
 Gln Val Xaa
 50

10

(2) INFORMATION FOR SEQ ID NO: 158:

(i) SEQUENCE CHARACTERISTICS:
 15 (A) LENGTH: 17 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:

20 Pro Asn Ser Phe Ser Cys Leu Gly Leu Ala Gly Thr Gly Ala Gly Ile
 1 5 10 15
 Xaa

25

(2) INFORMATION FOR SEQ ID NO: 159:

30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 53 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:

35

Met Gly Arg Tyr His Phe Val Phe Leu Thr Phe Phe Phe Ser Thr Tyr
 1 5 10 15
 Ser Ser Cys Phe Tyr Pro Val Val Ser Gln Val Leu Tyr Leu Val Cys
 40 20 25 30
 Ser Cys Thr Ala Asp Arg Pro Leu Met Ala Pro Val Gly Ser Cys Leu
 35 40 45

45

Gly Gly Arg Asn Xaa
 50

50

(2) INFORMATION FOR SEQ ID NO: 160:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 64 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:

Met Phe Val Thr Leu Ser Ile Leu Asn Ile Thr Ile Glu Lys Asp Lys
 1 5 10 15

60

292

Ser Thr Asn Arg Phe Arg Asp Val Phe Leu Gln His Ile Leu Val Ile
 20 25 30
 5 Leu Met Pro Ser Leu Thr Tyr Cys Leu Ile Gly Gln His Leu Cys Ser
 35 40 45
 Phe Thr Arg Tyr Val Ser Leu Cys Tyr Ser Arg Cys His Ser Trp Xaa
 50 55 60

10

15 (2) INFORMATION FOR SEQ ID NO: 161:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:

Met Ser Ile Cys Pro Leu Leu Val Met Leu Ile Leu Ile Thr Trp Val
 1 5 10 15
 25 Arg Cys Pro Val Ser Pro Val Tyr Arg Tyr Cys Phe Ser Phe Cys Asn
 20 25 30
 Xaa

30

35 (2) INFORMATION FOR SEQ ID NO: 162:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 95 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:

Met Gln Asp Ile Val Tyr Lys Leu Val Pro Gly Leu Gln Glu Gly Glu
 1 5 10 15
 45 Cys Leu Thr Val Leu Leu Ile Pro Glu Val Pro Ala Trp Pro Leu Gln
 20 25 30
 Pro Leu Leu Ser Trp Lys Phe Gly Ser Arg Met Gly Gly Pro Phe Pro
 35 40 45
 50 Phe Gly Arg Ile Thr Val Phe Ser Ser Leu Leu Ser Ala Gln Leu His
 50 55 60
 55 Leu Leu Gly Trp Ser Leu Leu Ser Ser Lys Met Arg Xaa His Leu Phe
 65 70 75 80
 Thr Pro Tyr Val Tyr Ser Phe Ser Lys Tyr Gly Ser His Val Xaa
 85 90 95

60

(2) INFORMATION FOR SEQ ID NO: 163:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 58 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:

10 Met Lys Val Leu Ala Thr Ser Phe Val Leu Gly Ser Leu Gly Leu Ala
1 5 10 15
Phe Tyr Leu Pro Leu Val Val Thr Thr Pro Lys Thr Leu Ala Ile Pro
20 25 30
15 Xaa Glu Ala Ala Arg Ser Cys Gly Glu Ser Tyr His Gln Cys His Asn
35 40 45
Leu Tyr Cys His Leu Trp Pro Trp Leu Xaa
20 50 55

(2) INFORMATION FOR SEQ ID NO: 164:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 44 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:

30 Met Asp Tyr Gly Tyr Tyr Ser Ala Gly Gln Phe Leu Leu His Leu Phe
1 5 10 15
35 Leu Ala Asp Leu Thr Gln Ala Thr Thr Gln Gln Lys Thr Asn Thr Ser
20 25 30
Glu Asn Gly Cys Lys Phe Val Cys Ala Val Phe Xaa
35 40
40

(2) INFORMATION FOR SEQ ID NO: 165:

(i) SEQUENCE CHARACTERISTICS:

- 45 (A) LENGTH: 18 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:

50 Gly Ile Val Leu Leu Ile Gly Val Leu Val Gln Val Ser Ala Val Asp
1 5 10 15
Asp Xaa
55

(2) INFORMATION FOR SEQ ID NO: 166:

60

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 166:

Met Gly Asn Ala Phe Glu Val Thr Gly Leu Met Leu Ala Leu Leu Cys
 1 5 10 15

10 Tyr Val Val Asp Gly Gln Lys Pro Lys Xaa Gly Phe Xaa Xaa
 20 25 30

15 (2) INFORMATION FOR SEQ ID NO: 167:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 37 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 167:

Met Ser His Glu Lys Ser Asn Glu Leu Val Leu Leu Ile Val Thr Val
 1 5 10 15

25 Met Arg Ser Leu Thr Tyr Asn Ile Ala Val Val Ala Ala Trp Phe Asn
 20 25 30

30 Gly Cys Ile Arg Xaa
 35

35 (2) INFORMATION FOR SEQ ID NO: 168:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 40 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168:

Met Tyr Leu Leu Tyr Leu Pro Ser Ala Leu Leu Pro Pro Tyr Pro Thr
 1 5 10 15

45 Cys Pro Tyr Glu His Gly Ser Pro Trp Pro His Thr Pro Ala Lys Leu
 20 25 30

50 Leu Cys Cys Phe Ala Phe Leu Xaa
 35 40

(2) INFORMATION FOR SEQ ID NO: 169:

55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 47 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

60 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169:

Met Lys Phe Ile Val Trp Arg Arg Phe Lys Trp Val Ile Ile Gly Leu
 1 5 10 15

5 Leu Phe Leu Leu Ile Leu Leu Leu Phe Val Ala Val Leu Leu Tyr Ser
 20 25 30

Leu Pro Asn Tyr Leu Ser Met Lys Ile Val Lys Pro Asn Val Xaa
 35 40 45

10

(2) INFORMATION FOR SEQ ID NO: 170:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 34 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

20 Ile Glu Trp Ser Gly Tyr Asn Lys Pro Glu Arg Lys Gly Pro Leu Ala
 1 5 10 15

Leu Phe Leu Val Phe Leu Phe Leu Asp Thr Pro Pro Leu Gln Gly Asp
 20 25 30

25

Leu Xaa

30

(2) INFORMATION FOR SEQ ID NO: 171:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 171:

40 Met Ser Leu Leu Xaa
 1 5

45 (2) INFORMATION FOR SEQ ID NO: 172:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 25 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 172:

Met Gln Leu Leu Ile Val Trp Asn Glu Ser Leu Thr Asn Ser Val Pro
 1 5 10 15

55 Ala Ser Val Asp Thr Ser Gln Cys Xaa
 20 25

60 (2) INFORMATION FOR SEQ ID NO: 173:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 262 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 173:

5 Met Ala Leu Gly Leu Lys Cys Phe Arg Met Val His Pro Thr Phe Arg
 1 5 10 15
 10 Asn Tyr Leu Ala Ala Ser Ile Arg Pro Val Ser Glu Val Thr Leu Lys
 20 25 30
 15 Thr Val His Glu Arg Gln His Gly His Arg Gln Tyr Met Ala Tyr Ser
 35 40 45
 Ala Val Pro Val Arg His Phe Ala Thr Lys Lys Ala Lys Ala Lys Gly
 50 55 60
 20 Lys Gly Gln Ser Gln Thr Arg Val Asn Ile Asn Ala Ala Leu Val Glu
 65 70 75 80
 Asp Ile Ile Asn Leu Glu Glu Val Asn Glu Glu Met Lys Ser Val Ile
 85 90 95
 25 Glu Ala Leu Lys Asp Asn Phe Asn Lys Thr Leu Asn Ile Arg Thr Ser
 100 105 110
 30 Pro Gly Ser Leu Asp Lys Ile Ala Val Val Thr Ala Asp Gly Lys Leu
 115 120 125
 Ala Leu Asn Gln Ile Ser Gln Ile Ser Met Lys Ser Pro Gln Leu Ile
 130 135 140
 35 Leu Val Asn Met Ala Ser Phe Pro Glu Cys Thr Ala Ala Ala Ile Lys
 145 150 155 160
 Ala Ile Arg Glu Ser Gly Met Asn Leu Asn Pro Glu Val Glu Gly Thr
 165 170 175
 40 Leu Ile Arg Val Pro Ile Pro Gln Val Thr Arg Glu His Arg Glu Met
 180 185 190
 45 Leu Val Lys Leu Ala Lys Gln Asn Thr Asn Lys Ala Lys Asp Ser Leu
 195 200 205
 Arg Lys Val Arg Thr Asn Ser Met Asn Lys Leu Lys Lys Ser Lys Asp
 210 215 220
 50 Thr Val Ser Glu Asp Thr Ile Arg Leu Ile Glu Lys Gln Ile Ser Gln
 225 230 235 240
 Met Ala Asp Asp Thr Val Ala Glu Leu Asp Arg His Leu Ala Val Lys
 245 250 255
 55 Thr Lys Glu Leu Leu Gly
 260
 60

(2) INFORMATION FOR SEQ ID NO: 174:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 967 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 174:

5 Met Gln Arg Ala Val Pro Glu Gly Phe Gly Arg Arg Lys Leu Gly Ser
 10 1 5 10 15
 Asp Met Gly Asn Ala Glu Arg Ala Pro Gly Ser Arg Ser Phe Gly Pro
 20 25 30
 15 Val Pro Thr Leu Leu Leu Leu Xaa Ala Ala Leu Leu Xaa Val Ser Asp
 35 40 45
 Ala Leu Gly Arg Pro Ser Glu Glu Asp Glu Glu Leu Val Val Pro Glu
 50 55 60
 20 Leu Glu Arg Ala Pro Gly His Gly Thr Thr Arg Leu Arg Leu His Ala
 65 70 75 80
 Phe Asp Gln Gln Leu Asp Leu Glu Leu Arg Pro Asp Ser Ser Phe Leu
 85 90 95
 25 Ala Pro Gly Phe Thr Leu Gln Asn Val Gly Arg Lys Ser Gly Ser Glu
 100 105 110
 30 Thr Pro Leu Pro Glu Thr Asp Leu Ala His Cys Phe Tyr Ser Gly Thr
 115 120 125
 Val Asn Gly Asp Pro Ser Ser Ala Ala Ala Leu Ser Leu Cys Glu Gly
 130 135 140
 35 Val Arg Gly Ala Phe Tyr Leu Leu Gly Glu Ala Tyr Phe Ile Gln Pro
 145 150 155 160
 Leu Pro Ala Ala Ser Glu Arg Leu Xaa Thr Ala Ala Pro Gly Glu Lys
 165 170 175
 40 Pro Pro Ala Pro Leu Gln Phe His Leu Leu Arg Arg Asn Arg Gln Gly
 180 185 190
 45 Asp Val Gly Gly Thr Cys Gly Val Val Asp Asp Glu Pro Arg Pro Thr
 195 200 205
 Gly Lys Ala Glu Thr Glu Asp Glu Asp Glu Gly Thr Glu Gly Glu Asp
 210 215 220
 50 Glu Gly Pro Gln Trp Ser Pro Gln Asp Pro Ala Leu Gln Gly Val Gly
 225 230 235 240
 Gln Pro Thr Gly Thr Gly Ser Ile Arg Lys Lys Arg Phe Val Ser Ser
 245 250 255
 55 His Arg Tyr Val Glu Thr Met Leu Val Ala Asp Gln Ser Met Ala Glu
 260 265 270
 60 Phe His Gly Ser Gly Leu Lys His Tyr Leu Leu Thr Leu Phe Ser Val

| | 275 | 280 | 285 |
|----|---|-------------------------------------|---------|
| | Ala Ala Arg Leu Xaa Lys His | Pro Xaa Ile Arg Asn Ser Val Ser Leu | |
| | 290 | 295 | 300 |
| 5 | Val Val Val Lys Ile Leu Val Ile His Asp Glu Gln Lys Gly Pro Glu | | |
| | 305 | 310 | 315 320 |
| 10 | Val Thr Ser Asn Ala Ala Leu Thr Leu Arg Asn Phe Cys Asn Trp Gln | | |
| | 325 | 330 | 335 |
| | Lys Gln His Asn Pro Pro Ser Asp Arg Asp Ala Glu His Tyr Asp Thr | | |
| | 340 | 345 | 350 |
| 15 | Ala Ile Leu Phe Thr Arg Gln Asp Leu Cys Gly Ser Gln Thr Cys Asp | | |
| | 355 | 360 | 365 |
| | Thr Leu Gly Met Ala Asp Val Gly Thr Val Cys Asp Pro Ser Arg Ser | | |
| 20 | 370 | 375 | 380 |
| | Cys Ser Val Ile Glu Asp Asp Gly Leu Gln Ala Ala Phe Thr Thr Ala | | |
| | 385 | 390 | 395 400 |
| 25 | His Glu Leu Gly His Val Phe Asn Met Pro His Asp Asp Ala Lys Gln | | |
| | 405 | 410 | 415 |
| | Cys Ala Ser Leu Asn Gly Val Asn Gln Asp Ser His Met Met Ala Ser | | |
| | 420 | 425 | 430 |
| 30 | Met Leu Ser Asn Leu Asp His Ser Gln Pro Trp Ser Pro Cys Ser Ala | | |
| | 435 | 440 | 445 |
| | Tyr Met Ile Thr Ser Phe Leu Asp Asn Gly His Gly Glu Cys Leu Met | | |
| 35 | 450 | 455 | 460 |
| | Asp Lys Pro Gln Asn Pro Ile Gln Leu Pro Gly Asp Leu Pro Gly Thr | | |
| | 465 | 470 | 475 480 |
| 40 | Ser Tyr Asp Ala Asn Arg Gln Cys Gln Phe Thr Phe Gly Glu Asp Ser | | |
| | 485 | 490 | 495 |
| | Lys His Cys Pro Asp Ala Ala Ser Thr Cys Ser Thr Leu Trp Cys Thr | | |
| | 500 | 505 | 510 |
| 45 | Gly Thr Ser Gly Gly Val Leu Val Cys Gln Thr Lys His Phe Pro Trp | | |
| | 515 | 520 | 525 |
| | Ala Asp Gly Thr Ser Cys Gly Glu Gly Lys Trp Cys Ile Asn Gly Lys | | |
| 50 | 530 | 535 | 540 |
| | Cys Val Xaa Lys Thr Asp Arg Lys His Phe Asp Thr Pro Phe His Gly | | |
| | 545 | 550 | 555 560 |
| 55 | Ser Trp Gly Met Trp Gly Pro Trp Gly Asp Cys Ser Arg Thr Cys Gly | | |
| | 565 | 570 | 575 |
| | Gly Gly Val Gln Tyr Thr Met Arg Glu Cys Asp Asn Pro Val Pro Lys | | |
| | 580 | 585 | 590 |
| 60 | Asn Gly Gly Lys Tyr Cys Glu Gly Lys Arg Val Arg Tyr Arg Ser Cys | | |

| | | | |
|----|---|-----|---------|
| | 595 | 600 | 605 |
| | Asn Leu Glu Asp Cys Pro Asp Asn Asn Gly Lys Thr Phe Arg Glu Glu | | |
| | 610 | 615 | 620 |
| 5 | Gln Cys Glu Ala His Asn Glu Phe Ser Lys Ala Ser Phe Gly Ser Gly | | |
| | 625 | 630 | 635 640 |
| 10 | Pro Ala Val Glu Trp Ile Pro Lys Tyr Ala Gly Val Ser Pro Lys Asp | | |
| | 645 | 650 | 655 |
| | Arg Cys Lys Leu Ile Cys Gln Ala Lys Gly Ile Gly Tyr Phe Phe Val | | |
| | 660 | 665 | 670 |
| 15 | Leu Gln Pro Lys Val Val Asp Gly Thr Pro Cys Ser Pro Asp Ser Thr | | |
| | 675 | 680 | 685 |
| | Ser Val Cys Val Gln Gly Gln Cys Val Lys Ala Gly Cys Asp Arg Ile | | |
| 20 | 690 | 695 | 700 |
| | Ile Asp Ser Lys Lys Lys Phe Asp Lys Cys Gly Val Cys Gly Gly Asn | | |
| | 705 | 710 | 715 720 |
| 25 | Gly Ser Thr Cys Lys Lys Ile Ser Gly Ser Val Thr Ser Ala Lys Pro | | |
| | 725 | 730 | 735 |
| | Gly Tyr His Asp Ile Ile Thr Ile Pro Thr Gly Ala Thr Asn Ile Glu | | |
| | 740 | 745 | 750 |
| 30 | Val Lys Gln Arg Asn Gln Arg Gly Ser Arg Asn Asn Gly Ser Phe Leu | | |
| | 755 | 760 | 765 |
| | Ala Ile Lys Ala Ala Asp Gly Thr Tyr Ile Leu Asn Gly Asp Tyr Thr | | |
| 35 | 770 | 775 | 780 |
| | Leu Ser Thr Leu Glu Gln Asp Ile Met Tyr Lys Gly Val Val Leu Arg | | |
| | 785 | 790 | 795 800 |
| 40 | Tyr Ser Gly Ser Ser Ala Ala Leu Glu Arg Ile Arg Ser Phe Ser Pro | | |
| | 805 | 810 | 815 |
| | Leu Lys Glu Pro Leu Thr Ile Gln Val Leu Thr Val Gly Asn Ala Leu | | |
| | 820 | 825 | 830 |
| 45 | Arg Pro Lys Ile Lys Tyr Thr Tyr Phe Val Lys Lys Lys Lys Glu Ser | | |
| | 835 | 840 | 845 |
| | Phe Asn Ala Ile Pro Thr Phe Ser Ala Trp Val Ile Glu Glu Trp Gly | | |
| 50 | 850 | 855 | 860 |
| | Glu Cys Ser Lys Ser Cys Glu Leu Gly Trp Gln Arg Arg Leu Val Glu | | |
| | 865 | 870 | 875 880 |
| 55 | Cys Arg Asp Ile Asn Gly Gln Pro Ala Ser Glu Cys Ala Lys Glu Val | | |
| | 885 | 890 | 895 |
| | Lys Pro Ala Ser Thr Arg Pro Cys Ala Asp His Pro Cys Pro Gln Trp | | |
| | 900 | 905 | 910 |
| 60 | Gln Leu Gly Glu Trp Ser Ser Cys Ser Lys Thr Cys Gly Lys Gly Tyr | | |

300

915 920 925
 Lys Lys Arg Ser Leu Lys Cys Leu Ser His Asp Gly Gly Val Leu Ser
 930 935 940
 5 His Glu Ser Cys Asp Pro Leu Lys Lys Pro Lys His Phe Ile Asp Phe
 945 950 955 960
 10 Cys Thr Met Ala Glu Cys Ser
 965

15 (2) INFORMATION FOR SEQ ID NO: 175:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 19 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 175:

Met Leu Lys Ile Pro Thr His Leu Glu Gly Lys Ile Lys Ile Thr Lys
 1 5 10 15
 25 Val Tyr Xaa

30 (2) INFORMATION FOR SEQ ID NO: 176:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 205 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 176:

Met Tyr Glu Thr Met Lys Leu Asp Ala Cys Xaa His Gln Gln Arg Pro
 1 5 10 15
 40 Thr Leu Gln Ala Gly Pro Lys Leu Leu Thr Leu Ala Pro Arg Glu Glu
 20 25 30
 45 Pro Arg Gly Gln Ser Gly Arg Gly Ser Glu Leu Thr Ala Arg Gln Arg
 35 40 45
 His Ser Thr Gly Asp Pro Gln Gly Glu Gln Ala Leu Pro Arg Ala Gly
 50 55 60
 50 Cys Val Thr Gly Pro Pro Ala Thr Pro His Arg Pro Ser Glu Pro Gln
 65 70 75 80
 Leu Leu Arg Thr His Pro Asp Ala Arg Pro Lys Ser Ala Met Ala Gln
 85 90 95
 55 Thr Phe Val His Gln Gly Pro Val Ala Leu Gln Gln Leu Thr Thr Asn
 100 105 110
 60 Arg Arg Val Glu Thr Ser Met Ser Ser Asp Gly His Gly Gln Asn Pro
 115 120 125

Thr Pro Ser Pro Trp Ala Asp Val Cys Ala Ser Arg Ala Asp Ala Val
 130 135 140
 5 Ala Phe Pro Ala Ser Gly Xaa Cys His Ser Pro Trp Leu Met Xaa Pro
 145 150 155 160
 Ser Ser His Pro Leu Asn Pro His Ser Pro Leu Asn Leu Pro Pro Pro
 165 170 175
 10 Ser Phe His Cys Lys Asp Pro Val Met Thr Leu His Pro Gln Thr Leu
 180 185 190
 Val Thr Gln Gly His Leu Ser Thr Ser Gly Arg Leu Thr
 195 200 205
 15

(2) INFORMATION FOR SEQ ID NO: 177:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 54 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 177:

Met Asp Ser Met Pro Glu Pro Ala Ser Arg Cys Leu Leu Leu Leu Pro
 1 5 10 15
 30 Leu Leu Leu Leu Leu Leu Leu Leu Leu Pro Ala Pro Glu Leu Gly Pro
 20 25 30
 Ser Gln Ala Gly Ala Glu Glu Asn Asp Trp Val Arg Leu Pro Ser Lys
 35 40 45
 35 Cys Glu Gly Thr Cys Gly
 50

40

(2) INFORMATION FOR SEQ ID NO: 178:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 436 amino acids

45

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 178:

Met Pro Leu Phe Leu Leu Ser Leu Pro Thr Pro Pro Ser Ala Ser Gly
 1 5 10 15
 His Glu Arg Arg Gln Arg Pro Glu Ala Lys Thr Ser Gly Ser Glu Lys
 20 25 30
 55 Lys Tyr Leu Arg Ala Met Gln Ala Asn Arg Ser Gln Leu His Ser Pro
 35 40 45
 Pro Gly Thr Gly Ser Ser Glu Asp Ala Ser Thr Pro Gln Cys Val His
 50 55 60
 60

302

Thr Arg Leu Thr Gly Glu Gly Ser Cys Pro His Ser Gly Asp Val His
 65 70 75 80
 5 Ile Gln Ile Asn Ser Ile Pro Lys Glu Cys Ala Glu Asn Ala Ser Ser
 85 90 95
 Arg Asn Ile Arg Ser Gly Val His Ser Cys Ala His Gly Cys Val His
 100 105 110
 10 Ser Arg Leu Arg Gly His Ser His Ser Glu Ala Arg Leu Thr Asp Asp
 115 120 125
 Thr Ala Ala Glu Ser Gly Asp His Gly Ser Ser Ser Phe Ser Glu Phe
 130 135 140
 15 Arg Tyr Leu Phe Lys Trp Leu Gln Lys Ser Leu Pro Tyr Ile Leu Ile
 145 150 155 160
 Leu Ser Val Lys Leu Val Met Gln His Ile Thr Gly Ile Ser Leu Gly
 165 170 175
 20 Ile Gly Leu Leu Thr Thr Phe Met Tyr Ala Asn Lys Ser Ile Val Asn
 180 185 190
 25 Gln Val Phe Leu Arg Glu Arg Ser Ser Lys Ile Gln Cys Ala Trp Leu
 195 200 205
 Leu Val Phe Leu Ala Gly Ser Ser Val Leu Leu Tyr Tyr Thr Phe His
 210 215 220
 30 Ser Gln Ser Leu Tyr Tyr Ser Leu Ile Phe Leu Asn Pro Thr Leu Asp
 225 230 235 240
 His Leu Ser Phe Trp Glu Val Phe Xaa Ile Val Gly Xaa Thr Asp Phe
 245 250 255
 35 Ile Leu Lys Phe Phe Phe Met Gly Leu Lys Cys Leu Ile Leu Leu Val
 260 265 270
 40 Pro Ser Phe Ile Met Pro Phe Lys Ser Lys Gly Tyr Trp Tyr Met Leu
 275 280 285
 Leu Glu Glu Leu Cys Gln Tyr Tyr Arg Thr Phe Val Pro Ile Pro Val
 290 295 300
 45 Trp Phe Arg Tyr Leu Ile Ser Tyr Gly Glu Phe Gly Xaa Val Thr Arg
 305 310 315 320
 Trp Xaa Leu Gly Ile Leu Leu Ala Leu Leu Tyr Leu Ile Leu Lys Leu
 325 330 335
 50 Leu Glu Phe Phe Gly His Leu Arg Thr Phe Arg Gln Val Leu Arg Ile
 340 345 350
 55 Phe Phe Thr Xaa Pro Ser Tyr Gly Val Ala Ala Ser Lys Arg Gln Cys
 355 360 365
 Ser Asp Val Asp Asp Ile Cys Ser Ile Cys Gln Ala Glu Phe Gln Lys
 370 375 380
 60

303

Pro Ile Leu Leu Ile Cys Gln His Ile Phe Cys Glu Glu Cys Met Thr
 385 390 395 400

5 Leu Trp Phe Asn Arg Glu Lys Thr Cys Pro Leu Cys Arg Thr Val Ile
 405 410 415

Ser Asp His Ile Asn Lys Trp Lys Asp Gly Ala Thr Ser Ser His Leu
 420 425 430

10 Gln Ile Tyr Xaa
 435

15 (2) INFORMATION FOR SEQ ID NO: 179:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 175 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 179:

Val Val Phe Gly Ala Ser Leu Phe Leu Leu Leu Ser Leu Thr Val Phe
 1 5 10 15

25 Ser Ile Val Ser Val Thr Ala Tyr Ile Ala Leu Ala Leu Leu Ser Val
 20 25 30

30 Thr Ile Ser Phe Arg Ile Tyr Lys Gly Val Ile Gln Ala Ile Gln Lys
 35 40 45

Ser Asp Glu Gly His Pro Phe Arg Ala Tyr Leu Glu Ser Glu Val Ala
 50 55 60

35 Ile Ser Glu Glu Leu Val Gln Lys Tyr Ser Asn Ser Ala Leu Gly His
 65 70 75 80

Val Asn Cys Thr Ile Lys Glu Leu Arg Arg Leu Phe Leu Val Asp Asp
 85 90 95

40 Leu Val Asp Ser Leu Lys Phe Ala Val Leu Met Trp Val Phe Thr Tyr
 100 105 110

Val Gly Ala Leu Phe Asn Gly Leu Thr Leu Leu Ile Leu Ala Leu Ile
 115 120 125

Ser Leu Phe Ser Val Pro Val Ile Tyr Glu Arg His Gln Ala Gln Ile
 130 135 140

50 Asp His Tyr Leu Gly Leu Ala Asn Lys Asn Val Lys Asp Ala Met Ala
 145 150 155 160

Lys Ile Gln Ala Lys Ile Pro Gly Leu Lys Arg Lys Ala Glu Xaa
 165 170 175

55

(2) INFORMATION FOR SEQ ID NO: 180:

60 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 219 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 180:

5 Met Glu Ala Pro Gly Ala Pro Pro Arg Thr Leu Thr Trp Glu Ala Met
1 5 10 15

10 Glu Gln Ile Arg Tyr Leu His Glu Glu Phe Pro Glu Ser Trp Ser Val
20 25 30

Pro Arg Leu Ala Glu Gly Phe Asp Val Ser Thr Asp Val Ile Arg Arg
35 40 45

15 Val Leu Lys Ser Lys Phe Leu Pro Thr Leu Glu Gln Lys Leu Lys Gln
50 55 60

Asp Gln Lys Val Leu Lys Lys Ala Gly Leu Ala His Ser Leu Gln His
65 70 75 80

20 Leu Arg Gly Ser Gly Asn Thr Ser Lys Leu Leu Pro Ala Gly His Ser
85 90 95

Val Ser Gly Ser Leu Leu Met Pro Gly His Glu Ala Ser Ser Lys Asp
100 105 110

Pro Asn His Ser Thr Ala Leu Lys Val Ile Glu Ser Asp Thr His Arg
115 120 125

30 Thr Asn Thr Pro Arg Arg Arg Lys Gly Arg Asn Lys Glu Ile Gln Asp
130 135 140

Leu Glu Glu Ser Phe Val Pro Val Ala Ala Pro Leu Gly His Pro Arg
145 150 155 160

35 Glu Leu Gln Lys Tyr Ser Ser Asp Ser Glu Ser Pro Arg Gly Thr Gly
165 170 175

Ser Gly Ala Leu Pro Ser Gly Gln Lys Leu Glu Glu Leu Lys Ala Glu
180 185 190

40 Glu Pro Asp Asn Phe Ser Ser Lys Val Val Gln Arg Gly Arg Glu Phe
195 200 205

45 Phe Asp Ser Asn Gly Asn Phe Leu Tyr Arg Ile
210 215

50 (2) INFORMATION FOR SEQ ID NO: 181:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 6 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 181:

Trp Lys Ala Glu Leu Xaa
1 5

60

(2) INFORMATION FOR SEQ ID NO: 182:

- 5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 44 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 182:

10 Met Ser Asn Thr Leu Leu Ser Gln Trp Leu Leu Leu Leu Thr Leu Phe
 1 5 10 15
 15 Lys Cys Ile Ile Leu Pro Leu Asn Leu Xaa Pro Ile Ile Arg Thr Ile
 20 25 30
 Pro Asp Trp Ser Pro Glu Leu Gly Thr Asn Thr Xaa
 35 40

20

(2) INFORMATION FOR SEQ ID NO: 183:

- 25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 59 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 183:

30 Met Trp Gln Val Arg Arg Gly Gly Cys Val Leu Ala Val Cys Ser Gln
 1 5 10 15
 Ala Arg Gly Thr Gly Gly Arg Leu Gly Trp Val Gly Thr Ser Ser Leu
 20 25 30
 35 Arg Val Arg Met Ala Glu Ser Thr Ser Leu Met Ser Gln Gly Arg Ser
 35 40 45
 Pro Ile Pro Arg Met Thr Pro Ala Arg Pro Xaa
 40 50 55

(2) INFORMATION FOR SEQ ID NO: 184:

- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 588 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 184:

Met Arg Asp Ala Gly Asp Pro Ser Pro Pro Asn Lys Met Leu Arg Arg
 1 5 10 15
 55 Ser Asp Ser Pro Glu Asn Lys Tyr Ser Asp Ser Thr Gly His Ser Lys
 20 25 30
 Ala Lys Asn Val His Thr His Arg Val Arg Glu Arg Asp Gly Gly Thr
 35 40 45

60

Ser Tyr Ser Pro Gln Glu Asn Ser His Asn His Ser Ala Leu His Ser
 50 55 60
 Ser Asn Ser His Ser Ser Asn Pro Ser Asn Asn Pro Ser Lys Thr Ser
 5 65 70 75 80
 Asp Ala Pro Tyr Asp Ser Ala Asp Asp Trp Ser Glu His Ile Ser Ser
 85 90 95
 10 Ser Gly Lys Lys Tyr Tyr Tyr Asn Cys Arg Thr Glu Val Ser Gln Trp
 100 105 110
 Glu Lys Pro Lys Glu Trp Leu Glu Arg Glu Gln Arg Gln Lys Glu Ala
 115 120 125
 15 Asn Lys Met Ala Val Asn Ser Phe Pro Lys Asp Arg Asp Tyr Arg Arg
 130 135 140
 Glu Val Met Gln Ala Thr Ala Thr Ser Gly Phe Ala Ser Gly Met Glu
 145 150 155 160
 20 Asp Lys His Ser Ser Asp Ala Ser Ser Leu Leu Pro Gln Asn Ile Leu
 165 170 175
 25 Ser Gln Thr Ser Arg His Asn Asp Arg Asp Tyr Arg Leu Pro Arg Ala
 180 185 190
 Glu Thr His Ser Ser Ser Thr Pro Val Gln His Pro Ile Lys Pro Val
 195 200 205
 30 Val His Pro Thr Ala Thr Pro Ser Thr Val Pro Ser Ser Pro Phe Thr
 210 215 220
 Leu Gln Ser Asp His Gln Pro Lys Lys Ser Phe Asp Ala Asn Gly Ala
 225 230 235 240
 35 Ser Thr Leu Ser Lys Leu Pro Thr Pro Thr Ser Ser Val Pro Ala Gln
 245 250 255
 40 Lys Thr Glu Arg Lys Glu Ser Thr Ser Gly Asp Lys Pro Val Ser His
 260 265 270
 Ser Cys Thr Thr Pro Ser Thr Ser Ser Ala Ser Gly Leu Asn Pro Thr
 275 280 285
 45 Ser Ala Pro Pro Thr Ser Ala Ser Ala Val Pro Val Ser Pro Val Pro
 290 295 300
 Gln Ser Pro Ile Pro Pro Leu Leu Gln Asp Pro Asn Leu Leu Arg Gln
 305 310 315 320
 50 Leu Leu Pro Ala Leu Gln Ala Thr Leu Gln Leu Asn Asn Ser Asn Val
 325 330 335
 55 Asp Ile Ser Lys Ile Asn Glu Val Leu Thr Ala Ala Val Thr Gln Ala
 340 345 350
 Ser Leu Gln Ser Ile Ile His Lys Phe Leu Thr Ala Gly Pro Ser Ala
 355 360 365
 60

307

Phe Asn Ile Thr Ser Leu Ile Ser Gln Ala Ala Gln Leu Ser Thr Gln
 370 375 380
 5 Ala Gln Pro Ser Asn Gln Ser Pro Met Ser Leu Thr Ser Asp Ala Ser
 385 390 395 400
 Ser Pro Arg Ser Tyr Val Ser Pro Arg Ile Ser Thr Pro Gln Thr Asn
 405 410 415
 10 Thr Val Pro Ile Lys Pro Leu Ile Ser Thr Pro Pro Val Ser Ser Gln
 420 425 430
 Pro Lys Val Ser Thr Pro Val Val Lys Gln Gly Pro Val Ser Gln Ser
 435 440 445
 15 Ala Thr Gln Gln Pro Val Thr Ala Asp Lys Xaa Gln Gly His Glu Pro
 450 455 460
 Val Ser Pro Arg Ser Leu Gln Arg Ser Ser Ser Gln Arg Ser Pro Ser
 20 465 470 475 480
 Pro Gly Pro Asn His Thr Ser Asn Ser Ser Asn Ala Ser Asn Ala Thr
 485 490 495
 25 Val Val Pro Gln Asn Ser Ser Ala Arg Ser Thr Cys Ser Leu Thr Pro
 500 505 510
 Ala Leu Ala Ala His Phe Ser Glu Asn Leu Ile Lys His Val Gln Gly
 515 520 525
 30 Trp Pro Ala Asp His Ala Glu Lys Gln Ala Ser Arg Leu Arg Glu Glu
 530 535 540
 Ala His Asn Met Gly Thr Ile His Met Ser Glu Ile Cys Thr Glu Leu
 35 545 550 555 560
 Lys Asn Leu Arg Ser Leu Val Arg Val Cys Glu Ile Gln Ala Thr Leu
 565 570 575
 40 Arg Glu Gln Arg Asp Thr Ile Phe Glu Thr Thr Asn
 580 585
 45 (2) INFORMATION FOR SEQ ID NO: 185:
 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 166 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 185:
 Met Asn Ile Lys His Leu Val Asp Pro Ile Asp Asp Leu Phe Leu Ala
 1 5 10 15
 55 Ala Lys Lys Ile Pro Gly Ile Ser Ser Thr Gly Val Gly Asp Gly Gly
 20 25 30
 Asn Glu Leu Gly Met Gly Lys Val Lys Glu Ala Val Arg Arg His Ile
 60 35 40 45

Arg His Gly Asp Val Ile Ala Cys Asp Val Glu Ala Asp Phe Ala Val
 50 55 60
 5 Ile Ala Gly Val Ser Asn Trp Gly Gly Tyr Ala Leu Ala Cys Ala Leu
 65 70 75 80
 Tyr Ile Leu Tyr Ser Cys Ala Val His Ser Gln Tyr Leu Arg Lys Ala
 85 90 95
 10 Val Gly Pro Ser Arg Ala Pro Gly Asp Gln Ala Trp Thr Gln Ala Leu
 100 105 110
 Pro Ser Val Ile Lys Glu Glu Lys Met Leu Gly Ile Leu Val Gln His
 115 120 125
 15 Lys Val Arg Ser Gly Val Ser Gly Ile Val Gly Met Glu Val Asp Gly
 130 135 140
 20 Leu Pro Phe His Asn Xaa His Ala Glu Met Ile Gln Lys Leu Val Asp
 145 150 155 160
 Val Thr Thr Ala Gln Val
 165
 25

(2) INFORMATION FOR SEQ ID NO: 186:

30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 9 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 186:

35 Met Leu Ile Leu Phe Leu Lys Lys Xaa
 1 5

40

(2) INFORMATION FOR SEQ ID NO: 187:

45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 20 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 187:

50 Thr His Thr His Thr His Pro Lys Ser Phe Tyr Ile Ile Lys Leu Ser
 1 5 10 15
 Tyr Tyr Tyr Xaa
 20

55

(2) INFORMATION FOR SEQ ID NO: 188:

60 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 32 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 188:

5 Met Ile Gln Ser Gly Leu Ile Ala Ile Leu Leu Ser Phe Leu Lys Val
 1 5 10 15
 Tyr Val Glu Gly Arg Pro Cys Val Cys Phe Ser Lys Gly Leu Xaa Xaa
 20 25 30

10

15

(2) INFORMATION FOR SEQ ID NO: 189:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 19 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 189:

25 Tyr Ile Tyr Leu Ile Val Tyr Ile Ser Phe Tyr Ser Phe Arg Pro Gln
 1 5 10 15
 Gln Leu Xaa

30

(2) INFORMATION FOR SEQ ID NO: 190:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 190:

40 Met Arg Phe Leu Leu Thr Val Trp Gly Ser Phe Pro Phe Met Leu Ile
 1 5 10 15
 Pro Val Phe Leu Ser Ile Gly Thr Lys Glu Met Lys Lys Ala Gln Arg
 20 25 30
 45 Xaa

50

(2) INFORMATION FOR SEQ ID NO: 191:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 84 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 191:

60 Met Arg Val Pro Pro Val Leu Arg Gly Arg Ile Leu Pro Leu Val Leu
 1 5 10 15

Gln Cys Thr Leu Leu Glu Phe Cys Leu Cys Ala Thr Thr Val Leu Pro
 20 25 30
 5 Thr Val Xaa Cys Trp Lys Pro Arg Leu Pro Val Xaa Ala Ser Gly Leu
 35 40 45
 Tyr Val Asp Arg Met Ser Leu Trp Lys Tyr Gly Cys Ser Gly Trp Asn
 50 55 60
 10 Glu Ser Ala Arg Pro Arg Arg Ala Gly Gly Thr Met Arg Pro Pro Arg
 65 70 75 80
 15 Ser Gly Arg Xaa

(2) INFORMATION FOR SEQ ID NO: 192:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 123 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 192:

Met Ala Gly Ala Phe Val Ala Val Phe Leu Leu Ala Met Phe Tyr Glu
 1 5 10 15
 30 Gly Leu Lys Ile Ala Arg Glu Ser Leu Leu Arg Lys Ser Gln Val Ser
 20 25 30
 Ile Arg Tyr Asn Ser Met Pro Val Pro Gly Pro Asn Gly Thr Ile Leu
 35 40 45
 35 Met Glu Thr His Lys Thr Val Gly Gln Gln Met Leu Ser Phe Pro His
 50 55 60
 40 Leu Leu Gln Thr Val Leu His Ile Ile Gln Val Val Ile Ser Tyr Phe
 65 70 75 80
 Leu Met Leu Ile Phe Met Thr Tyr Asn Gly Tyr Leu Cys Ile Ala Xaa
 85 90 95
 45 Ala Ala Gly Ala Gly Thr Gly Tyr Phe Leu Phe Ser Trp Lys Lys Ala
 100 105 110
 Val Val Val Asp Ile Thr Glu His Cys His Xaa
 115 120
 50

(2) INFORMATION FOR SEQ ID NO: 193:

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 143 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 193:

311

Met Gly Cys Leu Val Trp Gly Pro Ser Trp Pro Pro Leu Ser Leu Leu
 1 5 10 15

Ala Ser Leu Leu His Ser Gly Ile Ala Gly Arg Cys Leu Leu Cys Leu
 5 20 25 30

Phe Lys Gly Leu Ala Ala Ala Ala Ser Leu Gln Ile Arg Asp Leu Ala
 35 40 45

10 Ser Arg Leu Thr Thr Gly Pro Arg Thr Cys Arg Val Gln Pro Pro Pro
 50 55 60

His Pro Gln Ser Ser Pro Pro Trp Pro Gly Pro Pro Gly Ala Glu Thr
 65 70 75 80

15 Cys Arg Pro Leu Ser Arg Thr Val Gly Gly Val Cys Pro Ser Asp Trp
 85 90 95

Pro Val Ser Trp Leu Leu Leu Pro Pro Leu Pro Glu Val Val Thr Cys
 20 100 105 110

Ser Cys Pro Arg Ile Lys Ala Arg Pro Glu Arg Thr Pro Glu Leu Leu
 115 120 125

25 Cys Ala Trp Gly Gly Arg Gly Lys His Ser Gln Leu Val Ala Xaa
 130 135 140

30 (2) INFORMATION FOR SEQ ID NO: 194:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 51 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 194:

Met Pro Asn Val Met Leu Thr Leu Phe Val Met Thr Leu Ser Ser Ala
 1 5 10 15

40 Ser Asn Leu Gly Leu Tyr Phe Phe Lys Phe Asn Phe Glu Cys Ser Cys
 20 25 30

45 Met Phe Gly Thr Ser Leu Leu Thr Ala Lys Asp Lys Leu Phe Ile Cys
 35 40 45

Ile Thr Xaa
 50

50

(2) INFORMATION FOR SEQ ID NO: 195:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 222 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 195:

60 Met Ser Leu Leu Val Leu Val Leu Ser Trp Gly Ser Met Gly Leu Glu

[illegible]

(2) INFORMATION FOR SEQ ID NO: 196:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 102 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 196:

Met Ser Gln Leu Ser Arg Thr Ser Leu Ser Leu Leu Thr Leu Leu
1 5 10 15

55 Val Leu Trp Gly Ser Ser Cys Cys Leu Pro Ile Trp Cys Leu Pro Asn
20 25 30

Arg His Arg Leu Leu Lys Leu Ser Phe Leu Leu Phe Ser Pro Asp Ile
35 40 45

60

Pro Tyr Leu Ser His Thr His Pro Asn Asn Ile Ser Cys Ser Val Leu
 50 55 60

5 Ser Leu Arg Gln His Leu Asn Phe Thr Gln Pro Gly Ala Leu Phe Thr
 65 70 75 80

Cys Leu Val Gln Ile Gln Phe Gly Leu Ile Leu Gln Pro Cys Ile Ser
 85 90 95

10 Lys Trp Gly Leu Gly Xaa
 100

15 (2) INFORMATION FOR SEQ ID NO: 197:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 13 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 197:

Met Ile Ala Leu Phe Phe Val Thr Thr Xaa Leu Thr Xaa
 1 5 10

25

(2) INFORMATION FOR SEQ ID NO: 198:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 61 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 198:

Met Thr Tyr His Pro Asn Gln Val Val Glu Gly Cys Cys Ser Asp Met
 1 5 10 15

Ala Val Thr Phe Asn Gly Leu Thr Pro Asn Gln Met His Val Met Met
 20 25 30

Tyr Gly Val Tyr Arg Leu Arg Ala Phe Gly His Ile Phe Asn Asp Ala
 35 40 45

45 Leu Val Phe Leu Pro Pro Asn Gly Ser Asp Asn Asp Xaa
 50 55 60

50 (2) INFORMATION FOR SEQ ID NO: 199:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 71 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 199:

Met Ser Ser Ser Ser Leu His Trp Lys Glu Phe Lys Tyr Ala Pro Gly
 1 5 10 15

60

Ser Leu His Tyr Phe Ala Leu Ser Phe Val Leu Ile Leu Thr Glu Ile
 20 25 30
 5 Cys Leu Val Ser Ser Gly Met Gly Phe Pro Gln Glu Gly Lys His Phe
 35 40 45
 Ser Val Leu Gly Ser Pro Asp Cys Ser Leu Trp Gly Arg Asp Glu His
 50 55 60
 10 Val Pro Arg Glu Phe Ala Xaa
 65 70

15 (2) INFORMATION FOR SEQ ID NO: 200:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 10 amino acids

(B) TYPE: amino acid

20 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 200:

Met His Leu Arg Phe Pro Phe Leu Cys Xaa
 1 5 10

25

(2) INFORMATION FOR SEQ ID NO: 201:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 50 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 201:

Met Arg Arg Val Ala Arg Gly Arg Gly Leu Ala Leu Pro Ser Leu Glu
 1 5 10 15

40 His Arg Pro Ser Cys Ser Tyr Asp Ala Leu Pro Leu Pro Phe Cys Glu
 20 25 30

Thr Arg Asn Pro Glu Ala His Leu Tyr Phe Phe Arg Thr Asp Val Glu
 35 40 45

45 Arg Xaa
 50

50 (2) INFORMATION FOR SEQ ID NO: 202:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 13 amino acids

(B) TYPE: amino acid

55 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 202:

Ala Lys Ile Leu Val Phe Ile Phe Leu Phe Glu Leu Xaa
 1 5 10

60

(2) INFORMATION FOR SEQ ID NO: 203:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 38 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 203:

10

Met Phe Gln Glu Cys Ile Pro Ile Ser Leu Phe Phe Leu Asn Trp Leu
 1 5 10 15

15

Lys Glu Cys Cys Ser Phe Thr Cys Pro Asn Ser His Ile Asn Asn Cys
 20 25 30

Leu Thr Gly Ile Arg Xaa
 35

20

(2) INFORMATION FOR SEQ ID NO: 204:

25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 204:

30

Met Asn Phe Val Leu Phe Phe Ile Gly Ile Asn Val Gly Cys Arg Gly
 1 5 10 15

Glu Asn Ser Leu Lys Tyr Phe Thr Val Thr Val Xaa Cys Ser Pro Arg
 20 25 30

35

Asp Xaa

40

(2) INFORMATION FOR SEQ ID NO: 205:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 205:

50

Met Leu Leu Phe Leu Phe Val Cys Leu Pro Ile Thr Trp Met Ala Glu
 1 5 10 15

Phe Leu Ser Gln Leu Arg His Leu Leu Xaa
 20 25

55

(2) INFORMATION FOR SEQ ID NO: 206:

60

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 105 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 206:

5 Met Pro Arg His Ser Leu Tyr Ile Ile Ile Gly Ala Leu Cys Val Ala
 1 5 10 15
 Phe Ile Leu Met Leu Ile Ile Leu Ile Val Gly Ile Cys Arg Ile Ser
 20 25 30
 10 Arg Ile Glu Tyr Gln Gly Ser Ser Arg Pro Ala Tyr Glu Glu Phe Tyr
 35 40 45
 Asn Cys Arg Ser Ile Asp Ser Glu Phe Ser Asn Ala Ile Ala Ser Ile
 15 50 55 60
 Arg His Ala Arg Phe Gly Lys Lys Ser Arg Pro Ala Met Tyr Asp Val
 65 70 75 80
 20 Ser Pro Ile Ala Tyr Glu Asp Tyr Ser Pro Asp Asp Lys Pro Leu Val
 85 90 95
 Thr Leu Ile Lys Thr Lys Asp Leu Xaa
 100 105
 25

(2) INFORMATION FOR SEQ ID NO: 207:

30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 64 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 207:

35 Leu Lys Ser Cys Leu Leu Leu Val Ser Phe Leu Ser Gly Arg Val Pro
 1 5 10 15
 40 Ser Tyr Asp Leu Ile Tyr Val Cys Ser Ile Ala Leu Glu Thr Gly Phe
 20 25 30
 Val Cys Glu Met Ala Leu Ser Phe Val Asp His Phe Cys Arg Glu Ile
 35 40 45
 45 Val Asp Leu Gly Arg Ala Glu Ala Thr Ala Asp Met Pro Gly Val Xaa
 50 55 60
 50

(2) INFORMATION FOR SEQ ID NO: 208:

55 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 42 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 208:
 60

317

Met Ser Ala Trp Leu Pro Ser Pro Pro His Leu Leu Leu Leu Ser Ala
 1 5 10 15

5 Ala Ala Gly Ser Gly Ala Ser His Leu Arg Ala Leu Gly Ser Ser Ala
 20 25 30

Leu Glu Gly Leu Gln Asp Pro Ser Gln Xaa
 35 40

10

(2) INFORMATION FOR SEQ ID NO: 209:

15 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 42 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 209:

20 Met Ser Ser Pro Ala Thr Trp Arg Leu Thr Leu Pro Ser Leu Leu Val
 1 5 10 15

Phe Leu Thr Gly Glu Ala Met Pro Trp Pro Ala His Ser Thr Ser Cys
 20 25 30

25 Thr His Val Leu Ser Thr Val Ser Thr Xaa
 35 40

30

(2) INFORMATION FOR SEQ ID NO: 210:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 46 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 210:

40 Met Gln Ala Pro Leu Gln Asp Cys Gly Arg Ser Val Ser Leu Arg Leu
 1 5 10 15

Ala Cys Val Leu Ala Pro Leu Thr Thr Ser Ser Arg Gly Cys His Leu
 20 25 30

45 Gln Leu Pro Gln Asp Lys Gly Lys Ala Arg Xaa Asp Ser Xaa
 35 40 45

50 (2) INFORMATION FOR SEQ ID NO: 211:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 266 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 211:

Met Asn Gly Ser His Lys Asp Pro Leu Leu Pro Phe Pro Ala Ser Ala
 1 5 10 15

60

318

Arg Thr Pro Ser Leu Pro Pro Ala Pro Pro Ala Gln Ala Pro Leu Pro
 20 25 30
 5 Trp Lys Pro Ser Gly Phe Ala Arg Ile Ser Pro Pro Pro Pro Leu Ala
 35 40 45
 Ile Leu Gln Tyr Arg Gly Lys Ala Asp His Gly Glu Ser Gly Gln Gln
 50 55 60
 10 Leu Ala Ala Ala Pro Gly Asp Gly Arg Leu Pro Leu Leu Glu Ala Val
 65 70 75 80
 Arg Arg Leu Arg Gly Gln Asp Cys Gly Pro Leu Ser Ala Leu Cys His
 85 90 95
 15 Gly Gln Leu Leu Ala Gln Pro Val Pro Gln Val Leu Leu Leu Pro Gly
 100 105 110
 Ala Xaa Gly Asp Ile Gly Thr Ser Cys Tyr Thr Lys Ser Gly Met Ile
 115 120 125
 20 Leu Cys Arg Asn Asp Tyr Ile Arg Leu Phe Gly Asn Ser Gly Ala Cys
 130 135 140
 25 Ser Ala Cys Gly Gln Ser Ile Pro Ala Ser Glu Leu Val Met Arg Ala
 145 150 155 160
 Gln Gly Asn Val Tyr His Leu Lys Cys Phe Thr Cys Ser Thr Cys Arg
 165 170 175
 30 Asn Arg Leu Val Pro Gly Asp Arg Phe His Tyr Ile Asn Gly Ser Leu
 180 185 190
 Phe Cys Glu His Asp Arg Pro Thr Ala Leu Ile Asn Gly His Leu Asn
 195 200 205
 35 Ser Leu Gln Ser Asn Pro Leu Leu Pro Asp Gln Lys Val Cys Lys Val
 210 215 220
 40 Arg Val Met Gln Asn Ala Cys Leu His Leu Arg Phe Val His His Arg
 225 230 235 240
 Trp Ile Pro Cys Xaa Phe Ser Arg Gln Val Thr Phe Val Ala Ser Thr
 245 250 255
 45 Ser Ala Ser Ser Met Pro Leu His Leu Leu
 260 265

50

(2) INFORMATION FOR SEQ ID NO: 212:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 94 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 212:

60

Met Ala Arg Thr Arg Thr Pro Ser Ser Pro Phe Leu Leu Leu Arg Glu
 1 5 10 15

Leu Pro Pro Ser Leu Gln Leu Arg Gln Pro Arg Arg Pro Phe Pro Gly
 20 25 30
 5 Ser Arg Ala Ala Ser Leu Ala Phe His Arg Arg Arg Leu Ser Gln Tyr
 35 40 45
 Cys Asn Ile Gly Glu Lys Gln Thr Met Val Asn Pro Gly Ser Ser Ser
 50 55 60
 10 Gln Pro Pro Pro Val Thr Ala Gly Ser Leu Ser Trp Lys Arg Cys Ala
 65 70 75 80
 15 Gly Cys Gly Gly Lys Ile Ala Asp Arg Phe Leu Leu Tyr Ala
 85 90

20 (2) INFORMATION FOR SEQ ID NO: 213:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 213:

Leu Phe Gly Asn Ser Gly Ala Cys Ser Ala Cys Gly Gln Ser Ile Pro
 1 5 10 15
 30 Ala Ser Glu Leu Val Met Arg Ala
 20

35 (2) INFORMATION FOR SEQ ID NO: 214:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 19 amino acids

(B) TYPE: amino acid

40 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 214:

His Asp Arg Pro Thr Ala Leu Ile Asn Gly His Leu Asn Ser Leu Gln
 1 5 10 15
 45 Ser Asn Pro

50 (2) INFORMATION FOR SEQ ID NO: 215:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 12 amino acids

55 (B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 215:

Leu Val Pro Gly Asp Arg Phe His Tyr Ile Asn Gly
 1 5 10

(2) INFORMATION FOR SEQ ID NO: 216:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 81 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 216:

Met Lys Tyr Met Gly Gly Cys Ala Lys Val Met Cys Lys Tyr Tyr Val
 1 5 10 15

Ile Leu Tyr Gln Gly Leu Glu Tyr Pro Leu Leu Xaa Ser Gly Asp Pro
 20 25 30

Glu Thr Ser Pro Pro Trp Ile Leu Arg Ala Asp Cys Ile Val Leu Ser
 35 40 45

Ser Arg Asn Phe His Ser Asn Xaa Gly Arg Leu Thr Ile Asn Lys Ile
 50 55 60

Tyr Val Ile Gly Gly Gly Lys Tyr Arg Gly Glu Val Thr Asn Gly Ala
 65 70 75 80

Lys

30

(2) INFORMATION FOR SEQ ID NO: 217:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 41 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 217:

Met Gly Gln Ser Glu Leu Tyr Ser Ser Ile Leu Arg Asn Leu Gly Val
 1 5 10 15

Leu Phe Leu Val Tyr Thr Arg Gly Gly Phe Leu Leu Ser Pro Leu Leu
 20 25 30

His Gly Thr Leu Thr Cys Ala His Ser
 35 40

50

(2) INFORMATION FOR SEQ ID NO: 218:

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 35 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 218:

Met Val Leu Leu Leu Leu Thr Val Ala Ser Tyr Thr Val Phe Trp Met
 1 5 10 15

60

Ile Gly Asp Val Leu Asp Ile Leu Phe Leu Trp Asn Phe Glu Tyr Thr
 20 25 30

5 Thr Leu Tyr
 35

10 (2) INFORMATION FOR SEQ ID NO: 219:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 38 amino acids

(B) TYPE: amino acid

15 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 219:

Met Glu Leu Tyr Asn Ser Leu Cys Pro Ile Cys Tyr Phe Ser Thr Val
 1 5 10 15

20 Leu Thr Thr Thr Tyr Tyr Ile Tyr Phe Val Tyr Ser Gln Ser Ser Xaa
 20 25 30

25 Ile Arg Met Lys Val Pro
 35

30 (2) INFORMATION FOR SEQ ID NO: 220:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 45 amino acids

(B) TYPE: amino acid

35 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 220:

Met Gln Ile Val Ile Val Leu Tyr Cys Val Arg Asn Lys Asp Lys Lys
 1 5 10 15

40 Lys Val Cys Thr Cys Ser Val Gln Thr Gln Phe Phe Phe Pro Ile Phe
 20 25 30

45 Pro Ile Leu Gly Cys Leu Asn Gly Cys Arg Thr Gln Glu
 35 40 45

(2) INFORMATION FOR SEQ ID NO: 221:

50 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 28 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 221:

Met Lys Tyr Met Gly Gly Cys Ala Lys Val Met Cys Lys Tyr Tyr Val
 1 5 10 15

60 Ile Leu Tyr Gln Gly Leu Glu Tyr Pro Leu Leu Xaa
 20 25

(2) INFORMATION FOR SEQ ID NO: 222:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 35 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 222:

Leu Glu Tyr Pro Leu Leu Xaa Ser Gly Asp Pro Glu Thr Ser Pro Pro
 1 5 10 15

15

Trp Ile Leu Arg Ala Asp Cys Ile Val Leu Ser Ser Arg Asn Phe His
 20 25 30

Ser Asn Xaa
 35

20

(2) INFORMATION FOR SEQ ID NO: 223:

25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 223:

Arg Asn Phe His Ser Asn Xaa Gly Arg Leu Thr Ile Asn Lys Ile Tyr
 1 5 10 15

35

Val Ile Gly Gly Gly Lys Tyr Arg Gly Glu Val Thr Asn Gly Ala Lys
 20 25 30

40

(2) INFORMATION FOR SEQ ID NO: 224:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 145 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 224:

50

Val Thr Asn Glu Met Ser Gln Gly Arg Gly Lys Tyr Asp Phe Tyr Ile
 1 5 10 15

Gly Leu Gly Leu Ala Met Ser Ser Ser Ile Phe Ile Gly Gly Ser Phe
 20 25 30

55

Ile Leu Lys Lys Lys Gly Leu Leu Arg Leu Ala Arg Lys Gly Ser Met
 35 40 45

60

Arg Ala Gly Gln Gly Gly His Ala Tyr Leu Lys Glu Trp Leu Trp Trp
 50 55 60

323

Ala Gly Leu Leu Ser Met Gly Ala Gly Glu Val Ala Asn Phe Ala Ala
 65 70 75 80

5 Tyr Ala Phe Ala Pro Ala Thr Leu Val Thr Pro Leu Gly Ala Leu Ser
 85 90 95

Val Leu Val Ser Ala Ile Leu Ser Ser Tyr Phe Leu Asn Glu Arg Leu
 100 105 110

10 Asn Leu His Gly Lys Ile Gly Cys Leu Leu Ser Ile Leu Gly Ser Thr
 115 120 125

Val Met Val Ile His Ala Pro Lys Glu Glu Glu Ile Glu Thr Leu Asn
 15 130 135 140

Glu
 145

20

(2) INFORMATION FOR SEQ ID NO: 225:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 78 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 225:

25 Val Thr Asn Glu Met Ser Gln Gly Arg Gly Lys Tyr Asp Phe Tyr Ile
 1 5 10 15

Gly Leu Gly Leu Ala Met Ser Ser Ser Ile Phe Ile Gly Gly Ser Phe
 20 25 30

35 Ile Leu Lys Lys Lys Gly Leu Leu Arg Leu Ala Arg Lys Gly Ser Met
 35 40 45

Arg Ala Gly Gln Gly Gly His Ala Tyr Leu Lys Glu Trp Leu Trp Trp
 40 50 55 60

Ala Gly Leu Leu Ser Met Gly Ala Gly Glu Val Ala Asn Phe
 65 70 75

45

(2) INFORMATION FOR SEQ ID NO: 226:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 30 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 226:

50 Asn Phe Ala Ala Tyr Ala Phe Ala Pro Ala Thr Leu Val Thr Pro Leu
 1 5 10 15

Gly Ala Leu Ser Val Leu Val Ser Ala Ile Leu Ser Ser Tyr
 20 25 30

60

(2) INFORMATION FOR SEQ ID NO: 227:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 36 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 227:

10

Glu Arg Leu Asn Leu His Gly Lys Ile Gly Cys Leu Leu Ser Ile Leu
1 5 10 15

15

Gly Ser Thr Val Met Val Ile His Ala Pro Lys Glu Glu Glu Ile Glu
20 25 30

Thr Leu Asn Glu
35

20

(2) INFORMATION FOR SEQ ID NO: 228:

25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 228:

30

Arg Phe Lys Thr Leu Met Thr Asn Lys Ser Glu Gln Asp Gly Asp Ser
1 5 10 15

35

Ser Lys Thr Ile Glu Ile Ser Asp Met Lys Tyr His Ile Phe Gln
20 25 30 -

(2) INFORMATION FOR SEQ ID NO: 229:

40

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 20 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 229:

45

Leu Val Glu Gly Lys Leu Phe Tyr Ala His Lys Val Leu Leu Val Thr
1 5 10 15

50

Xaa Ser Asn Arg
20

(2) INFORMATION FOR SEQ ID NO: 230:

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 87 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

60

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 230:

5 CCT:AAAAGC TGACATTTTA TAATTGTGTT GTATAGCAGC AACTATATCC TTCCAAAAAT 60
CAAATGTTTT TIGACCATTG TTCAGTT 87

10

(2) INFORMATION FOR SEQ ID NO: 231:

(i) SEQUENCE CHARACTERISTICS:

15

- (A) LENGTH: 38 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 231:

20

CCTTAAAAGC TGACATTTTA TAATTGTGTT GTATAGCA 38

25

(2) INFORMATION FOR SEQ ID NO: 232:

(i) SEQUENCE CHARACTERISTICS:

30

- (A) LENGTH: 38 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 232:

35

CTTCCAAAAA TCAAATGTTT TTTGACCATT GTTCAGTT 38

40

(2) INFORMATION FOR SEQ ID NO: 233:

(i) SEQUENCE CHARACTERISTICS:

45

- (A) LENGTH: 455 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 233:

50

Met Ala Gln His Phe Ser Leu Ala Ala Cys Asp Val Val Gly Phe Asp
1 5 10 15

Leu Asp His Thr Leu Cys Arg Tyr Asn Leu Pro Glu Ser Ala Pro Leu
20 25 30

55

Ile Tyr Asn Ser Phe Ala Gln Phe Leu Val Lys Glu Lys Gly Tyr Asp
35 40 45

Lys Glu Leu Leu Asn Val Thr Pro Glu Asp Trp Asp Phe Cys Cys Lys
50 55 60

60

| | | | | | | | | | | | | | | | | | |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| | Gly | Leu | Ala | Leu | Asp | Leu | Glu | Asp | Gly | Asn | Phe | Leu | Lys | Leu | Ala | Asn | |
| | 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
| 5 | Asn | Gly | Thr | Val | Leu | Arg | Ala | Ser | His | Gly | Thr | Lys | Met | Met | Thr | Pro | |
| | | | | | 85 | | | | | 90 | | | | | 95 | | |
| | Glu | Val | Leu | Ala | Glu | Ala | Tyr | Gly | Lys | Lys | Glu | Trp | Lys | His | Phe | Leu | |
| | | | | | 100 | | | | | 105 | | | | | 110 | | |
| 10 | Ser | Asp | Thr | Gly | Met | Ala | Cys | Arg | Ser | Gly | Lys | Tyr | Tyr | Phe | Tyr | Asp | |
| | | | | | 115 | | | | | 120 | | | | 125 | | | |
| | Asn | Tyr | Phe | Asp | Leu | Pro | Gly | Ala | Leu | Leu | Cys | Ala | Arg | Val | Val | Asp | |
| 15 | | | | | 130 | | | | | 135 | | | | 140 | | | |
| | Tyr | Leu | Thr | Lys | Leu | Asn | Asn | Gly | Gln | Lys | Thr | Phe | Asp | Phe | Trp | Lys | |
| | | | | | 145 | | | | | 150 | | | | 155 | | 160 | |
| 20 | Asp | Ile | Val | Ala | Ala | Ile | Gln | His | Asn | Tyr | Lys | Met | Ser | Ala | Phe | Lys | |
| | | | | | 165 | | | | | 170 | | | | | | 175 | |
| | Glu | Asn | Cys | Gly | Ile | Tyr | Phe | Pro | Glu | Ile | Lys | Arg | Asp | Pro | Gly | Arg | |
| | | | | | 180 | | | | | 185 | | | | | 190 | | |
| 25 | Tyr | Leu | His | Ser | Cys | Pro | Glu | Ser | Val | Lys | Lys | Trp | Leu | Arg | Gln | Leu | |
| | | | | | 195 | | | | | 200 | | | | 205 | | | |
| | Lys | Asn | Ala | Gly | Lys | Ile | Leu | Leu | Leu | Ile | Thr | Ser | Ser | His | Ser | Asp | |
| 30 | | | | | 210 | | | | | 215 | | | | 220 | | | |
| | Tyr | Cys | Arg | Leu | Leu | Cys | Glu | Tyr | Ile | Leu | Gly | Asn | Asp | Phe | Thr | Asp | |
| | | | | | 225 | | | | | 230 | | | | 235 | | 240 | |
| 35 | Leu | Phe | Asp | Ile | Val | Ile | Thr | Asn | Ala | Leu | Lys | Pro | Gly | Phe | Phe | Ser | |
| | | | | | 245 | | | | | 250 | | | | | 255 | | |
| | His | Leu | Pro | Ser | Gln | Arg | Pro | Phe | Arg | Thr | Leu | Glu | Asn | Asp | Glu | Glu | |
| | | | | | 260 | | | | | 265 | | | | | 270 | | |
| 40 | Gln | Glu | Ala | Leu | Pro | Ser | Leu | Asp | Lys | Pro | Gly | Trp | Tyr | Ser | Gln | Gly | |
| | | | | | 275 | | | | | 280 | | | | | 285 | | |
| | Asn | Ala | Val | His | Leu | Tyr | Glu | Leu | Leu | Lys | Lys | Met | Thr | Gly | Lys | Pro | |
| 45 | | | | | 290 | | | | | 295 | | | | 300 | | | |
| | Glu | Pro | Lys | Val | Val | Tyr | Phe | Gly | Asp | Ser | Met | His | Ser | Asp | Ile | Phe | |
| | | | | | 305 | | | | | 310 | | | | 315 | | 320 | |
| 50 | Pro | Ala | Arg | His | Tyr | Ser | Asn | Trp | Glu | Thr | Val | Leu | Ile | Leu | Glu | Glu | |
| | | | | | 325 | | | | | 330 | | | | | 335 | | |
| | Leu | Arg | Gly | Asp | Glu | Gly | Thr | Arg | Ser | Gln | Arg | Pro | Glu | Glu | Ser | Glu | |
| | | | | | 340 | | | | | 345 | | | | | 350 | | |
| 55 | Pro | Leu | Glu | Lys | Lys | Gly | Lys | Tyr | Glu | Gly | Pro | Lys | Ala | Lys | Pro | Leu | |
| | | | | | 355 | | | | | 360 | | | | 365 | | | |
| 60 | Asn | Thr | Ser | Ser | Lys | Lys | Trp | Gly | Ser | Phe | Phe | Ile | Asp | Ser | Val | Leu | |
| | | | | | 370 | | | | | 375 | | | | 380 | | | |

327

Gly Leu Glu Asn Thr Glu Asp Ser Leu Val Tyr Thr Trp Ser Cys Lys
 385 390 395 400
 5 Arg Ile Ser Thr Tyr Ser Thr Ile Ala Ile Pro Ser Ile Glu Ala Ile
 405 410 415
 Ala Glu Leu Pro Leu Asp Tyr Lys Phe Thr Arg Phe Ser Ser Ser Asn
 420 425 430
 10 Ser Lys Thr Ala Gly Tyr Tyr Pro Asn Pro Pro Leu Val Leu Ser Ser
 435 440 445
 Asp Glu Thr Leu Ile Ser Lys
 450 455
 15

(2) INFORMATION FOR SEQ ID NO: 234:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 27 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 234:

25 Thr Ser Ser His Ser Asp Tyr Cys Arg Leu Leu Cys Glu Tyr Ile Leu
 1 5 10 15
 Gly Asn Asp Phe Thr Asp Leu Phe Asp Ile Val
 30 20 25

(2) INFORMATION FOR SEQ ID NO: 235:

35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 327 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 235:

Met Lys Thr Lys Asn Ile Pro Glu Ala His Gln Asp Ala Phe Lys Thr
 1 5 10 15
 45 Gly Phe Ala Glu Gly Phe Leu Lys Ala Gln Ala Leu Thr Gln Lys Thr
 20 25 30
 Asn Asp Ser Leu Arg Arg Thr Arg Leu Ile Leu Phe Val Leu Leu Leu
 35 40 45
 50 Phe Gly Ile Tyr Gly Leu Leu Lys Asn Pro Phe Leu Ser Val Arg Phe
 50 55 60
 Arg Thr Thr Thr Gly Leu Asp Ser Ala Val Asp Pro Val Gln Met Lys
 55 65 70 75 80
 Asn Val Thr Phe Glu His Val Lys Gly Val Glu Glu Ala Lys Gln Glu
 85 90 95
 60 Leu Gln Glu Val Val Glu Phe Leu Lys Asn Pro Gln Lys Phe Thr Ile

328

100 105 110
 Leu Gly Gly Lys Leu Pro Lys Gly Ile Leu Leu Val Gly Pro Pro Gly
 115 120 125
 5 Thr Gly Lys Thr Leu Leu Ala Arg Ala Val Ala Gly Glu Ala Asp Val
 130 135 140
 10 Pro Phe Tyr Tyr Ala Ser Gly Ser Glu Phe Asp Glu Met Phe Val Gly
 145 150 155 160
 Val Gly Ala Ser Arg Ile Arg Asn Leu Phe Arg Glu Ala Lys Ala Asn
 165 170 175
 15 Ala Pro Cys Val Ile Phe Ile Asp Glu Leu Asp Ser Val Gly Gly Lys
 180 185 190
 Arg Ile Glu Ser Pro Met His Pro Tyr Ser Arg Gln Thr Ile Asn Gln
 195 200 205
 20 Leu Leu Ala Glu Met Asp Gly Phe Lys Pro Asn Glu Gly Val Ile Ile
 210 215 220
 Ile Gly Ala Thr Asn Phe Pro Glu Ala Leu Asp Asn Ala Leu Ile Arg
 225 230 235 240
 25 Pro Gly Arg Phe Asp Met Gln Val Thr Val Pro Arg Pro Asp Val Lys
 245 250 255
 30 Gly Arg Thr Glu Ile Leu Lys Trp Tyr Leu Asn Lys Ile Lys Phe Asp
 260 265 270
 Xaa Ser Val Asp Pro Glu Ile Ile Ala Arg Gly Thr Val Gly Phe Ser
 275 280 285
 35 Gly Ala Glu Leu Glu Asn Leu Val Asn Gln Ala Ala Leu Lys Ala Ala
 290 295 300
 Val Asp Gly Lys Glu Met Val Thr Met Lys Glu Leu Gly Val Phe Gln
 305 310 315 320
 40 Arg Gln Asn Ser Asn Gly Ala
 325
 45

(2) INFORMATION FOR SEQ ID NO: 236:

(i) SEQUENCE CHARACTERISTICS:

- 50 (A) LENGTH: 21 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 236:

55 Met Lys Thr Lys Asn Ile Pro Glu Ala His Gln Asp Ala Phe Lys Thr
 1 5 10 15
 Gly Phe Ala Glu Gly
 20
 60

(2) INFORMATION FOR SEQ ID NO: 237:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 237:

Pro Val Gln Met Lys Asn Val Thr Phe Glu His Val Lys Gly Val Glu
1 5 10 15

15

Glu Ala Lys Gln Glu Leu Gln
20

(2) INFORMATION FOR SEQ ID NO: 238:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 238:

Ser Arg Gln Thr Ile Asn Gln Leu Leu Ala Glu Met Asp Gly Phe Lys
1 5 10 15

30

Pro Asn Glu Gly Val Ile Ile
20

35

(2) INFORMATION FOR SEQ ID NO: 239:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 amino acids

(B) TYPE: amino acid

40

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 239:

Phe Ser Gly Ala Glu Leu Glu Asn Leu Val Asn Gln Ala Ala Leu Lys
1 5 10 15

45

Ala Ala Val Asp Gly Lys Glu Met
20

50

(2) INFORMATION FOR SEQ ID NO: 240:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 192 amino acids

55

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 240:

60

Leu Pro Met Trp Gln Val Thr Ala Phe Leu Asp His Asn Ile Val Thr
1 5 10 15

330

Ala Gln Thr Thr Trp Lys Gly Leu Trp Met Ser Cys Val Val Gln Ser
 20 25 30

5 Thr Gly His Met Gln Cys Lys Val Tyr Asp Ser Val Leu Ala Leu Ser
 35 40 45

Thr Glu Val Gln Ala Ala Arg Ala Leu Thr Val Ser Ala Val Leu Leu
 50 55 60

10 Ala Phe Val Ala Leu Phe Val Thr Leu Ala Gly Ala Gln Cys Thr Thr
 65 70 75 80

15 Cys Val Ala Pro Gly Pro Ala Lys Ala Arg Val Ala Leu Thr Gly Gly
 85 90 95

Val Leu Tyr Leu Phe Cys Gly Leu Leu Ala Leu Val Pro Leu Cys Trp
 100 105 110

20 Phe Ala Asn Ile Val Val Arg Glu Phe Tyr Asp Pro Ser Val Pro Val
 115 120 125

Ser Gln Lys Tyr Glu Leu Gly Ala Xaa Leu Tyr Ile Gly Trp Ala Ala
 130 135 140

25 Thr Ala Leu Leu Met Val Gly Gly Cys Leu Leu Cys Cys Gly Ala Trp
 145 150 155 160

Val Cys Thr Gly Arg Pro Asp Leu Ser Phe Pro Val Lys Tyr Ser Ala
 165 170 175

30 Pro Arg Arg Pro Thr Ala Thr Gly Asp Tyr Asp Lys Lys Asn Tyr Val
 180 185 190

35

40 (2) INFORMATION FOR SEQ ID NO: 241:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 24 amino acids

(B) TYPE: amino acid

45 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 241:

Leu His Tyr Phe Ala Leu Ser Phe Val Leu Ile Leu Thr Glu Ile Cys
 1 5 10 15

50

Leu Val Ser Ser Gly Met Gly Phe
 20

55

(2) INFORMATION FOR SEQ ID NO: 242:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

60 (B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 242:

5 Gln Leu Arg Asn Gly Ile Pro Pro Gly Arg Lys Ala Leu Phe Cys Ser
 1 5 10 15

 Gly Lys Pro Arg Leu Phe Thr Leu Gly Gln Gly Arg Thr Cys Ala
 20 25 30

10

(2) INFORMATION FOR SEQ ID NO: 243:

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 39 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 243:

20 Trp Ser Gly Leu Trp Val Thr Thr Trp Asn Gly Ser Ser Gly Glu Arg
 1 5 10 15

 Thr Pro Ser Pro Trp Arg Arg Lys Arg Ala Ser Gln Ser Ala Gly Arg
 20 25 30

25 Ile Ala Ser Trp Met Ser Phe
 35

30

(2) INFORMATION FOR SEQ ID NO: 244:

(i) SEQUENCE CHARACTERISTICS:

35

(A) LENGTH: 14 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 244:

40 Glu Tyr Asn Lys Glu Ser Glu Asp Lys Tyr Val Phe Leu Val
 1 5 10

(2) INFORMATION FOR SEQ ID NO: 245:

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 14 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 245:

 Ile Asp Val Glu Ile Ala Arg Ser Asp Cys Arg Lys Pro Leu
 1 5 10

55

(2) INFORMATION FOR SEQ ID NO: 246:

(i) SEQUENCE CHARACTERISTICS:

60

(A) LENGTH: 142 amino acids

332

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 246:

5 Met Pro Arg Cys Arg Trp Leu Ser Leu Ile Leu Leu Thr Ile Pro Leu
 1 5 10 15

Ala Leu Val Ala Arg Lys Asp Pro Lys Lys Asn Glu Thr Gly Val Leu
 20 25 30

10 Arg Lys Leu Lys Pro Val Asn Ala Ser Asn Ala Asn Val Lys Gln Cys
 35 40 45

15 Leu Trp Phe Ala Met Gln Glu Tyr Asn Lys Glu Ser Glu Asp Lys Tyr
 50 55 60

Val Phe Leu Val Val Lys Thr Leu Gln Ala Gln Leu Gln Val Thr Asn
 65 70 75 80

20 Leu Leu Glu Tyr Leu Ile Asp Val Glu Ile Ala Arg Ser Asp Cys Arg
 85 90 95

Lys Pro Leu Ser Thr Asn Glu Ile Cys Ala Ile Gln Glu Asn Ser Lys
 100 105 110

25 Leu Lys Arg Lys Leu Ser Cys Ser Phe Leu Val Gly Ala Leu Pro Trp
 115 120 125

30 Asn Gly Glu Phe Thr Val Met Glu Lys Lys Cys Glu Asp Ala
 130 135 140

(2) INFORMATION FOR SEQ ID NO: 247:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 92 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 247:

Cys Leu Trp Phe Ala Met Gln Glu Tyr Asn Lys Glu Ser Glu Asp Lys
 1 5 10 15

45 Tyr Val Phe Leu Val Val Lys Thr Leu Gln Ala Gln Leu Gln Val Thr
 20 25 30

Asn Leu Leu Glu Tyr Leu Ile Asp Val Glu Ile Ala Arg Ser Asp Cys
 35 40 45

50 Arg Lys Pro Leu Ser Thr Asn Glu Ile Cys Ala Ile Gln Glu Asn Ser
 50 55 60

55 Lys Leu Lys Arg Lys Leu Ser Cys Ser Phe Leu Val Gly Ala Leu Pro
 65 70 75 80

Trp Asn Gly Glu Phe Thr Val Met Glu Lys Lys Cys
 85 90

60

(2) INFORMATION FOR SEQ ID NO: 248:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 123 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 248:

10 Ala Arg Lys Asp Pro Lys Lys Asn Glu Thr Gly Val Leu Arg Lys Leu
1 5 10 15
Lys Pro Val Asn Ala Ser Asn Ala Asn Val Lys Gln Cys Leu Trp Phe
20 25 30
15 Ala Met Gln Glu Tyr Asn Lys Glu Ser Glu Asp Lys Tyr Val Phe Leu
35 40 45
Val Val Lys Thr Leu Gln Ala Gln Leu Gln Val Thr Asn Leu Leu Glu
20 50 55 60
Tyr Leu Ile Asp Val Glu Ile Ala Arg Ser Asp Cys Arg Lys Pro Leu
65 70 75 80
25 Ser Thr Asn Glu Ile Cys Ala Ile Gln Glu Asn Ser Lys Leu Lys Arg
85 90 95
Lys Leu Ser Cys Ser Phe Leu Val Gly Ala Leu Pro Trp Asn Gly Glu
100 105 110
30 Phe Thr Val Met Glu Lys Lys Cys Glu Asp Ala
115 120

35

(2) INFORMATION FOR SEQ ID NO: 249:

(i) SEQUENCE CHARACTERISTICS:

- 40 (A) LENGTH: 44 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 249:

45 Asp Ser Pro Asp Thr Glu Pro Gly Ser Ser Ala Gly Pro Thr Gln Arg
1 5 10 15
Pro Ser Asp Asn Ser His Asn Glu His Ala Pro Ala Ser Gln Gly Leu
20 25 30
50 Lys Ala Glu His Leu Tyr Ile Leu Ile Gly Val Ser
35 40

55 (2) INFORMATION FOR SEQ ID NO: 250:

(i) SEQUENCE CHARACTERISTICS:

- 60 (A) LENGTH: 101 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 250:

5 His Arg Gln Asn Gln Ile Lys Gln Gly Pro Pro Arg Ser Lys Asp Glu
 1 5 10 15
 Glu Gln Lys Pro Gln Gln Arg Pro Asp Leu Ala Val Asp Val Leu Glu
 20 25 30
 10 Arg Thr Ala Asp Lys Ala Thr Val Asn Gly Leu Pro Glu Lys Asp Arg
 35 40 45
 Glu Thr Asp Thr Ser Ala Leu Ala Ala Gly Ser Ser Gln Glu Val Thr
 50 55 60
 15 Tyr Ala Gln Leu Asp His Trp Ala Leu Thr Gln Arg Thr Ala Arg Ala
 65 70 75 80
 Val Ser Pro Gln Ser Thr Lys Pro Met Ala Glu Ser Ile Thr Tyr Ala
 85 90 95
 20 Ala Val Ala Arg His
 100

25

(2) INFORMATION FOR SEQ ID NO: 251:

(i) SEQUENCE CHARACTERISTICS:

30

(A) LENGTH: 115 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 251:

35 Met Ser Pro His Pro Thr Ala Leu Leu Gly Leu Val Leu Cys Leu Ala
 1 5 10 15
 Gln Thr Ile His Thr Gln Glu Glu Asp Leu Pro Arg Pro Ser Ile Ser
 20 25 30
 40 Ala Glu Pro Gly Thr Val Ile Pro Leu Gly Ser His Val Thr Phe Val
 35 40 45
 Cys Arg Gly Pro Val Gly Val Gln Thr Phe Arg Leu Glu Arg Glu Ser
 50 55 60
 45 Arg Ser Thr Tyr Asn Asp Thr Glu Asp Val Ser Gln Ala Ser Pro Ser
 65 70 75 80
 Glu Ser Glu Ala Arg Phe Arg Ile Asp Ser Val Ser Glu Gly Asn Ala
 85 90 95
 50 Gly Pro Tyr Arg Cys Ile Tyr Tyr Lys Pro Pro Lys Trp Ser Glu Gln
 100 105 110
 55 Ser Asp Tyr
 115

60

(2) INFORMATION FOR SEQ ID NO: 252:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 252:

Thr Ala Leu Leu Gly Leu Val Leu Cys Leu Ala Gln Thr Ile His Thr
1 5 10 15
Gln Glu

(2) INFORMATION FOR SEQ ID NO: 253:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 253:

Leu Pro Arg Pro Ser Ile Ser Ala Glu Pro Gly Thr Val Ile
1 5 10

(2) INFORMATION FOR SEQ ID NO: 254:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 254:

Cys Arg Gly Pro Val Gly Val Gln Thr Phe Arg Leu Glu Arg Glu
1 5 10 15

(2) INFORMATION FOR SEQ ID NO: 255:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 31 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 255:

Val Leu Glu Arg Thr Ala Asp Lys Ala Thr Val Asn Gly Leu Pro Glu
1 5 10 15

Lys Asp Arg Glu Thr Asp Thr Ser Ala Leu Ala Ala Gly Ser Ser
20 25 30

(2) INFORMATION FOR SEQ ID NO: 256:

(i) SEQUENCE CHARACTERISTICS:

336

(A) LENGTH: 438 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 256:

5 Met Asn Thr Pro Asn Gly Asn Ser Leu Ser Ala Ala Glu Leu Thr Cys
 1 5 10 15
 10 Gly Met Ile Met Cys Leu Ala Arg Gln Ile Pro Gln Ala Thr Ala Ser
 20 25 30
 Met Lys Asp Gly Lys Trp Glu Arg Lys Lys Phe Met Gly Thr Glu Leu
 35 40 45
 15 Asn Gly Lys Thr Leu Gly Ile Leu Gly Leu Gly Arg Ile Gly Arg Glu
 50 55 60
 Val Ala Thr Arg Met Gln Ser Phe Gly Met Lys Thr Ile Gly Tyr Asp
 65 70 75 80
 20 Pro Ile Ile Ser Pro Glu Val Ser Ala Ser Phe Gly Val Gln Gln Leu
 85 90 95
 Pro Leu Glu Glu Ile Trp Pro Leu Cys Asp Phe Ile Thr Val His Thr
 100 105 110
 Pro Leu Leu Pro Ser Thr Thr Gly Leu Leu Asn Asp Asn Thr Phe Ala
 115 120 125
 30 Gln Cys Lys Lys Gly Val Arg Val Val Asn Cys Ala Arg Gly Gly Ile
 130 135 140
 Val Asp Glu Gly Ala Leu Leu Arg Ala Leu Gln Ser Gly Gln Cys Ala
 145 150 155 160
 35 Gly Ala Ala Leu Asp Val Phe Thr Glu Glu Pro Pro Arg Asp Arg Ala
 165 170 175
 Leu Val Asp His Glu Asn Val Ile Ser Cys Pro His Leu Gly Ala Ser
 180 185 190
 Thr Lys Glu Ala Gln Ser Arg Cys Gly Glu Glu Ile Ala Val Gln Phe
 195 200 205
 45 Val Asp Met Val Lys Gly Lys Ser Leu Thr Gly Val Val Asn Ala Gln
 210 215 220
 Ala Leu Thr Ser Ala Phe Ser Pro His Thr Lys Pro Trp Ile Gly Leu
 225 230 235 240
 50 Ala Glu Ala Leu Gly Thr Leu Met Arg Ala Trp Ala Gly Ser Pro Lys
 245 250 255
 Gly Thr Ile Gln Val Ile Thr Gln Gly Thr Ser Leu Lys Asn Ala Gly
 260 265 270
 55 Asn Cys Leu Ser Pro Ala Val Ile Val Gly Leu Leu Lys Glu Ala Ser
 275 280 285
 60 Lys Gln Ala Asp Val Asn Leu Val Asn Ala Lys Leu Leu Val Lys Glu

337

290 295 300

Al: Gly Leu Asn Val Thr Thr Ser His Ser Pro Ala Ala Pro Gly Glu
 305 310 315 320

5 Gln Gly Phe Gly Glu Cys Leu Leu Ala Val Ala Leu Ala Gly Ala Pro
 325 330 335

10 Tyr Gln Ala Val Gly Leu Val Gln Gly Thr Thr Pro Val Leu Gln Gly
 340 345 350

Leu Asn Gly Ala Val Phe Arg Pro Glu Val Pro Leu Arg Arg Asp Leu
 355 360 365

15 Pro Leu Leu Leu Phe Arg Thr Gln Thr Ser Asp Pro Ala Met Leu Pro
 370 375 380

Thr Met Ile Gly Leu Leu Ala Glu Ala Gly Val Arg Leu Leu Ser Tyr
 385 390 395 400

20 Gln Thr Ser Leu Val Ser Asp Gly Glu Thr Trp His Val Met Gly Ile
 405 410 415

25 Ser Ser Leu Leu Pro Ser Leu Glu Ala Trp Lys Gln His Val Thr Glu
 420 425 430

Ala Phe Gln Phe His Phe
 435

30

(2) INFORMATION FOR SEQ ID NO: 257:

- 35 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 24 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 257:

40 Met Ala Phe Ala Asn Leu Arg Lys Val Leu Ile Ser Asp Ser Leu Asp
 1 5 10 15

Pro Cys Cys Arg Lys Ile Leu Gln
 20

45

(2) INFORMATION FOR SEQ ID NO: 258:

- 50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 18 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 258:

55 Gly Gly Leu Gln Val Val Glu Lys Gln Asn Leu Ser Lys Glu Glu Leu
 1 5 10 15

Ile Ala
 60

5 (2) INFORMATION FOR SEQ ID NO: 259:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 259:

Met Cys Leu Ala Arg Gln Ile Pro Gln Ala Thr Ala Ser Met Lys Asp
1 5 10 15

15 Gly Lys Trp Glu Arg Lys Lys Phe Met Gly Thr Glu Leu
20 25

20 (2) INFORMATION FOR SEQ ID NO: 260:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 260:

Ala Leu Thr Ser Ala Phe Ser Pro His Thr Lys Pro Trp Ile Gly Leu
1 5 10 15

30 Ala Glu Ala Leu Gly Thr Leu Met Arg Ala Trp Ala Gly
20 25

35 (2) INFORMATION FOR SEQ ID NO: 261:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 36 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 261:

Glu Val Pro Leu Arg Arg Asp Leu Pro Leu Leu Leu Phe Arg Thr Gln
1 5 10 15

45 Thr Ser Asp Pro Ala Met Leu Pro Thr Met Ile Gly Leu Leu Ala Glu
20 25 30

50 Ala Gly Val Arg
35

55 (2) INFORMATION FOR SEQ ID NO: 262:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 109 amino acids

(B) TYPE: amino acid

60 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 262:

5 Phe Gly Thr Arg Phe Leu Ala Asn Leu Leu Leu Glu Glu Asp Asn Lys
 1 5 10 15
 Phe Cys Ala Asp Cys Gln Ser Lys Gly Pro Arg Trp Ala Ser Trp Asn
 20 25 30
 10 Ile Gly Val Phe Ile Cys Ile Arg Cys Ala Xaa Ile His Arg Asn Leu
 35 40 45
 Gly Val His Ile Ser Arg Val Lys Ser Val Asn Leu Asp Gln Trp Thr
 50 55 60
 15 Gln Val Gln Ile Gln Cys Met Gln Xaa Met Gly Asn Gly Lys Ala Asn
 65 70 75 80
 Arg Leu Tyr Glu Ala Tyr Leu Pro Glu Thr Phe Arg Arg Pro Gln Ile
 85 90 95
 20 Asp Pro Ala Val Glu Gly Phe Ile Arg Asp Xaa Tyr Glu
 100 105

25

(2) INFORMATION FOR SEQ ID NO: 263:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 21 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 263:

35 Glu Glu Asp Asn Lys Phe Cys Ala Asp Cys Gln Ser Lys Gly Pro Arg
 1 5 10 15
 Trp Ala Ser Trp Asn
 20

40

(2) INFORMATION FOR SEQ ID NO: 264:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 20 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 264:

50 Gly Val Phe Ile Cys Ile Arg Cys Ala Xaa Ile His Arg Asn Leu Gly
 1 5 10 15
 Val His Ile Ser
 20

55

(2) INFORMATION FOR SEQ ID NO: 265:

60 (i) SEQUENCE CHARACTERISTICS:

340

(A) LENGTH: 23 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 265:

5

Ser Val Asn Leu Asp Gln Trp Thr Gln Val Gln Ile Gln Cys Met Gln
 1 5 10 15

10

Xaa Met Gly Asn Gly Lys Ala
 20

(2) INFORMATION FOR SEQ ID NO: 266:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 245 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 266:

Met Asp Leu Leu Gly Leu Asp Ala Pro Val Ala Cys Ser Ile Ala Asn
 1 5 10 15

25

Ser Lys Thr Ser Asn Thr Leu Glu Lys Asp Leu Asp Leu Leu Ala Ser
 20 25 30

Val Pro Ser Pro Ser Ser Ser Gly Ser Arg Lys Val Val Gly Ser Met
 35 40 45

30

Pro Thr Ala Gly Ser Ala Gly Ser Val Pro Glu Asn Leu Asn Leu Phe
 50 55 60

35

Pro Glu Pro Gly Ser Lys Ser Glu Glu Ile Gly Lys Lys Gln Leu Ser
 65 70 75 80

Lys Asp Ser Ile Leu Ser Leu Tyr Gly Ser Gln Thr Xaa Gln Met Pro
 85 90 95

40

Thr Gln Ala Met Phe Met Ala Pro Ala Gln Met Ala Tyr Pro Thr Ala
 100 105 110

Tyr Pro Ser Phe Pro Gly Val Thr Pro Pro Asn Ser Ile Met Gly Ser
 115 120 125

45

Met Met Pro Pro Pro Val Gly Met Val Ala Gln Pro Gly Ala Ser Gly
 130 135 140

50

Met Val Ala Pro Met Ala Met Pro Ala Gly Tyr Met Gly Gly Met Gln
 145 150 155 160

Ala Ser Met Met Gly Val Pro Asn Gly Met Met Thr Thr Gln Gln Ala
 165 170 175

55

Gly Tyr Met Ala Gly Met Ala Ala Met Pro Gln Thr Val Tyr Gly Val
 180 185 190

Gln Pro Ala Gln Gln Leu Gln Trp Asn Leu Thr Gln Met Thr Gln Gln
 195 200 205

60

Met Ala Gly Met Asn Phe Tyr Gly Ala Asn Gly Met Met Asn Tyr Gly
 210 215 220

Gln Ser Met Ser Gly Gly Asn Gly Gln Ala Ala Asn Gln Thr Leu Ser
 225 230 235 240

Pro Gln Met Trp Lys
 245

10

(2) INFORMATION FOR SEQ ID NO: 267:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 315 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 267:

Met Asp Leu Leu Gly Leu Asp Ala Pro Val Ala Cys Ser Ile Ala Asn
 1 5 10 15

Ser Lys Thr Ser Asn Thr Leu Glu Lys Asp Leu Asp Leu Leu Ala Ser
 20 25 30

Val Pro Ser Pro Ser Ser Ser Gly Ser Arg Lys Val Val Gly Ser Met
 35 40 45

Pro Thr Ala Gly Ser Ala Gly Ser Val Pro Glu Asn Leu Asn Leu Phe
 50 55 60

Pro Glu Pro Gly Ser Lys Ser Glu Glu Ile Gly Lys Lys Gln Leu Ser
 65 70 75 80

Lys Asp Ser Ile Leu Ser Leu Tyr Gly Ser Gln Thr Xaa Gln Met Pro
 85 90 95

Thr Gln Ala Met Phe Met Ala Pro Ala Gln Met Ala Tyr Pro Thr Ala
 100 105 110

Tyr Pro Ser Phe Pro Gly Val Thr Pro Pro Asn Ser Ile Met Gly Ser
 115 120 125

Met Met Pro Pro Pro Val Gly Met Val Ala Gln Pro Gly Ala Ser Gly
 130 135 140

Met Val Ala Pro Met Ala Met Pro Ala Gly Tyr Met Gly Gly Met Gln
 145 150 155 160

Ala Ser Met Met Gly Val Pro Asn Gly Met Met Thr Thr Gln Gln Ala
 165 170 175

Gly Tyr Met Ala Gly Met Ala Ala Met Pro Gln Thr Val Tyr Gly Val
 180 185 190

Gln Pro Ala Gln Gln Leu Gln Trp Asn Leu Thr Gln Met Thr Gln Gln
 195 200 205

Met Ala Gly Met Asn Phe Tyr Gly Ala Asn Gly Met Met Asn Tyr Gly
 210 215 220

342

Gln Ser Met Ser Gly Gly Asn Gly Gln Ala Ala Asn Gln Thr Leu Ser
 225 230 235 240

5 Pro Gln Met Trp Lys Phe Gly Thr Arg Phe Leu Ala Asn Leu Leu Leu
 245 250 255

Glu Glu Asp Asn Lys Phe Cys Ala Asp Cys Gln Ser Lys Gly Pro Arg
 260 265 270

10 Trp Ala Ser Trp Asn Ile Gly Val Phe Ile Cys Ile Arg Cys Ala Xaa
 275 280 285

Ile His Arg Asn Leu Gly Val His Ile Ser Arg Val Lys Ser Val Asn
 15 290 295 300

Leu Asp Gln Trp Thr Gln Val Gln Ile Gln Cys
 305 310 315

20

(2) INFORMATION FOR SEQ ID NO: 268:

(i) SEQUENCE CHARACTERISTICS:
 25 (A) LENGTH: 39 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 268:

30 Met Gln Xaa Met Gly Asn Gly Lys Ala Asn Arg Leu Tyr Glu Ala Tyr
 1 5 10 15

Leu Pro Glu Thr Phe Arg Arg Pro Gln Ile Asp Pro Ala Val Glu Gly
 20 25 30

35 Phe Ile Arg Asp Xaa Tyr Glu
 35

40

(2) INFORMATION FOR SEQ ID NO: 269:

(i) SEQUENCE CHARACTERISTICS:
 45 (A) LENGTH: 67 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 269:

50 Lys Tyr Gly Lys Val Gly Lys Cys Val Ile Phe Glu Ile Pro Gly Ala
 1 5 10 15

Pro Asp Asp Glu Ala Val Arg Ile Phe Leu Glu Phe Glu Arg Val Glu
 20 25 30

55 Ser Ala Ile Lys Ala Val Val Asp Leu Asn Gly Arg Tyr Phe Gly Gly
 35 40 45

Arg Val Val Lys Ala Cys Phe Tyr Asn Leu Asp Lys Phe Arg Val Leu
 50 55 60

60

Asp Leu Ala
65

5

(2) INFORMATION FOR SEQ ID NO: 270:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 12 amino acids

10

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 270:

Lys Ala Val Asp Leu Gly Arg Tyr Phe Gly Gly Arg
15 1 5 10

(2) INFORMATION FOR SEQ ID NO: 271:

20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 271:

Glu Ala Val Arg Ile Phe Phe Arg Glu
 1 5

30

(2) INFORMATION FOR SEQ ID NO: 272:

(i) SEQUENCE CHARACTERISTICS:

35

(A) LENGTH: 306 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 272:

40 Arg Met Gly Arg Phe His Arg Ile Leu Glu Pro Gly Leu Asn Ile Leu
 1 5 10 15

Ile Pro Val Leu Asp Arg Ile Arg Tyr Val Gln Ser Leu Lys Glu Ile
 20 25 30

45

Val Ile Asn Val Pro Glu Gln Ser Ala Val Thr Leu Asp Asn Val Thr
 35 40 45

50

Leu Gln Ile Asp Gly Val Leu Tyr Leu Arg Ile Met Asp Pro Tyr Lys
 50 55 60

Ala Ser Tyr Gly Val Glu Asp Pro Glu Tyr Ala Val Thr Gln Leu Ala
 65 70 75 80

55

Gln Thr Thr Met Arg Ser Glu Leu Gly Lys Leu Ser Leu Asp Lys Val
 85 90 95

Phe Arg Glu Arg Glu Ser Leu Asn Ala Ser Ile Val Asp Ala Ile Asn
 100 105 110

60

344

Gln Ala Ala Asp Cys Trp Gly Ile Arg Cys Leu Arg Tyr Glu Ile Lys
 115 120 125

5 Asp Ile His Val Pro Pro Arg Val Lys Glu Ser Met Gln Met Gln Val
 130 135 140

Glu Ala Glu Arg Arg Lys Arg Ala Thr Val Leu Glu Ser Glu Gly Thr
 145 150 155 160

10 Arg Glu Ser Ala Ile Asn Val Ala Glu Gly Lys Lys Gln Ala Gln Ile
 165 170 175

Leu Ala Ser Glu Ala Glu Lys Ala Glu Gln Ile Asn Gln Ala Ala Gly
 180 185 190

15 Glu Ala Ser Ala Val Leu Ala Lys Ala Lys Ala Lys Ala Glu Ala Ile
 195 200 205

Arg Ile Leu Ala Ala Ala Leu Thr Gln His Asn Gly Asp Ala Ala Ala
 210 215 220

Ser Leu Thr Val Ala Glu Gln Tyr Val Ser Ala Phe Ser Lys Leu Ala
 225 230 235 240

25 Lys Asp Ser Asn Thr Ile Leu Leu Pro Ser Asn Pro Gly Asp Val Thr
 245 250 255

Ser Met Val Ala Gln Ala Met Gly Val Tyr Gly Ala Leu Thr Lys Ala
 260 265 270

30 Pro Val Pro Gly Thr Pro Asp Ser Leu Ser Ser Gly Ser Ser Arg Asp
 275 280 285

Val Gln Gly Thr Asp Ala Ser Leu Asp Glu Glu Leu Asp Arg Val Lys
 290 295 300

35 Met Ser
 305

40

(2) INFORMATION FOR SEQ ID NO: 273:

- (i) SEQUENCE CHARACTERISTICS:
- 45 (A) LENGTH: 26 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 273:

50 Ala Ser Tyr Gly Val Glu Asp Pro Glu Tyr Ala Val Thr Gln Leu Ala
 1 5 10 15

Gln Thr Thr Met Arg Ser Glu Leu Gly Lys
 20 25

55

(2) INFORMATION FOR SEQ ID NO: 274:

- 60 (i) SEQUENCE CHARACTERISTICS:

345

(A) LENGTH: 27 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 274:

5

Met Gln Met Gln Val Glu Ala Glu Arg Arg Lys Arg Ala Thr Val Leu
 1 5 10 15

10

Glu Ser Glu Gly Thr Arg Glu Ser Ala Ile Asn
 20 25

(2) INFORMATION FOR SEQ ID NO: 275:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 275:

Leu Thr Val Ala Glu Gln Tyr Val Ser Ala Phe Ser Lys Leu Ala Lys
 1 5 10 15

25

Asp Ser Asn Thr Ile Leu Leu Pro Ser Asn
 20 25

30

(2) INFORMATION FOR SEQ ID NO: 276:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 70 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 276:

Leu Leu Gly Ala Thr Ala Pro Leu Val Ser Leu Val Pro Glu Val Ala
 1 5 10 15

40

Ala Ala Val Gly Asn Ala Gly Ala Arg Gly Ala Xaa His Trp Gly Pro
 20 25 30

45

Phe Ala Glu Gly Leu Ser Thr Gly Phe Trp Pro Arg Ser Ala Arg Ala
 35 40 45

Ser Ser Gly Leu Pro Arg Asn Thr Val Val Leu Phe Val Pro Gln Gln
 50 55 60

50

Glu Ala Trp Val Val Glu
 65 70

55

(2) INFORMATION FOR SEQ ID NO: 277:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 46 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 277:

5 Arg Met Trp Arg Asn Gly Thr His Phe Trp Glu Cys Lys Ile Val Gln
 1 5 10 15
 Pro Leu Trp Lys Thr Val Trp Trp Phe Pro Arg Lys Leu Ser Ile Glu
 20 25 30
 10 Leu Pro Glu Asn Leu Ala Ile Leu Ile Gly Thr Tyr Phe Lys
 35 40 45

(2) INFORMATION FOR SEQ ID NO: 278:

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 278:

25 Leu Lys Arg His Phe Pro Lys Glu Ala Asn Lys His Val Lys Arg Cys
 1 5 10 15
 Ser Thr Ser Leu Asp Ile Arg Glu Ile Gln Ile Lys Ile Lys Met Arg
 20 25 30

Tyr

30

(2) INFORMATION FOR SEQ ID NO: 279:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 328 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 279:

45 Gly Thr Arg Pro Gly Glu Ser His Ala Asn Asp Leu Glu Cys Ser Gly
 1 5 10 15
 Lys Gly Lys Cys Thr Thr Lys Pro Ser Glu Ala Thr Phe Ser Cys Thr
 20 25 30
 Cys Glu Glu Gln Tyr Val Gly Thr Phe Cys Glu Glu Tyr Asp Ala Cys
 35 40 45
 50 Gln Arg Lys Pro Cys Gln Asn Asn Ala Ser Cys Ile Asp Ala Asn Glu
 50 55 60
 Lys Gln Asp Gly Ser Asn Phe Thr Cys Val Cys Leu Pro Gly Tyr Thr
 65 70 75 80
 55 Gly Glu Leu Cys Gln Ser Lys Ile Asp Tyr Cys Ile Leu Asp Pro Cys
 85 90 95
 60 Arg Asn Gly Ala Thr Cys Ile Ser Ser Leu Ser Gly Phe Thr Cys Gln
 100 105 110

347

Cys Pro Glu Gly Tyr Phe Gly Ser Ala Cys Glu Glu Lys Val Asp Pro
 115 120 125
 5 Cys Ala Ser Ser Pro Cys Gln Asn Asn Gly Thr Cys Tyr Val Asp Gly
 130 135 140
 Val His Phe Thr Cys Asn Cys Ser Pro Gly Phe Thr Gly Pro Thr Cys
 145 150 155 160
 10 Ala Gln Leu Ile Asp Phe Cys Ala Leu Ser Pro Cys Ala His Gly Thr
 165 170 175
 Cys Arg Ser Val Gly Thr Ser Tyr Lys Cys Leu Cys Asp Pro Gly Tyr
 180 185 190
 His Gly Leu Tyr Cys Glu Glu Glu Tyr Asn Glu Cys Leu Ser Ala Pro
 195 200 205
 20 Cys Leu Asn Ala Ala Thr Cys Arg Asp Leu Val Asn Gly Tyr Glu Cys
 210 215 220
 Val Cys Leu Ala Glu Tyr Lys Gly Thr His Cys Glu Leu Tyr Lys Asp
 225 230 235 240
 25 Pro Cys Ala Asn Val Ser Cys Leu Asn Gly Ala Thr Cys Asp Ser Asp
 245 250 255
 Gly Leu Asn Gly Thr Cys Ile Cys Ala Pro Gly Phe Thr Gly Glu Glu
 260 265 270
 Cys Asp Ile Asp Ile Asn Glu Cys Asp Ser Asn Pro Cys His His Gly
 275 280 285
 35 Gly Ser Cys Leu Asp Gln Pro Asn Gly Tyr Asn Cys His Cys Pro His
 290 295 300
 Gly Trp Val Gly Ala Asn Cys Glu Ile His Leu Gln Trp Lys Ser Gly
 305 310 315 320
 40 His Met Ala Glu Ser Leu Thr Asn
 325

45

(2) INFORMATION FOR SEQ ID NO: 280:

(i) SEQUENCE CHARACTERISTICS:

50

(A) LENGTH: 25 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 280:

55

Gly Lys Cys Thr Thr Lys Pro Ser Glu Ala Thr Phe Ser Cys Thr Cys
 1 5 10 15

Glu Glu Gln Tyr Val Gly Thr Phe Cys
 20 25

60

(2) INFORMATION FOR SEQ ID NO: 281:

(i) SEQUENCE CHARACTERISTICS:

5

(A) LENGTH: 22 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 281:

10 Cys Ala His Gly Thr Cys Arg Ser Val Gly Thr Ser Tyr Lys Cys Leu
 1 5 10 15

Cys Asp Pro Gly Tyr His
 20

15

(2) INFORMATION FOR SEQ ID NO: 282:

(i) SEQUENCE CHARACTERISTICS:

20

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 282:

25

Cys Ala Asn Val Ser Cys Leu Asn Gly Ala Thr Cys Asp Ser Asp Gly
 1 5 10 15

30 Leu Asn Gly Thr Cys Ile Cys Ala Pro Gly Phe Thr Gly Glu Glu Cys
 20 25 30

Asp

35

(2) INFORMATION FOR SEQ ID NO: 283:

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 299 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 283:

45 Met Ala Gln Asn Leu Lys Asp Leu Ala Gly Arg Leu Pro Ala Gly Pro
 1 5 10 15

Arg Gly Met Gly Thr Ala Leu Lys Leu Leu Gly Ala Gly Ala Val
 20 25 30

50

Ala Tyr Gly Val Arg Glu Ser Val Phe Thr Val Glu Gly Gly His Arg
 35 40 45

55 Ala Ile Phe Phe Asn Arg Ile Gly Gly Val Gln Gln Asp Thr Ile Leu
 50 55 60

Ala Glu Gly Leu His Phe Arg Ile Pro Trp Phe Gln Tyr Pro Ile Ile
 65 70 75 80

60 Tyr Asp Ile Arg Ala Arg Pro Arg Lys Ile Ser Ser Pro Thr Gly Ser

349

85 90 95
 Lys Asp Leu Gln Met Val Asn Ile Ser Leu Arg Val Leu Ser Arg Pro
 100 105 110
 5 Asn Ala Gln Glu Leu Pro Ser Met Tyr Gln Arg Leu Gly Leu Asp Tyr
 115 120 125
 10 Glu Glu Arg Val Leu Pro Ser Ile Val Asn Glu Val Leu Lys Ser Val
 130 135 140
 Val Ala Lys Phe Asn Ala Ser Gln Leu Ile Thr Gln Arg Ala Gln Val
 145 150 155 160
 15 Ser Leu Leu Ile Arg Arg Glu Leu Thr Glu Arg Ala Lys Asp Phe Ser
 165 170 175
 Leu Ile Leu Asp Asp Val Ala Ile Thr Glu Leu Ser Phe Ser Arg Glu
 180 185 190
 20 Tyr Thr Ala Ala Val Glu Ala Lys Gln Val Ala Gln Gln Glu Ala Gln
 195 200 205
 25 Arg Ala Gln Phe Leu Val Glu Lys Ala Lys Gln Glu Gln Arg Gln Lys
 210 215 220
 Ile Val Gln Ala Glu Gly Glu Ala Glu Ala Ala Lys Met Leu Gly Glu
 225 230 235 240
 30 Ala Leu Ser Lys Asn Pro Gly Tyr Ile Lys Leu Arg Lys Ile Arg Ala
 245 250 255
 Ala Gln Asn Ile Ser Lys Thr Ile Ala Thr Ser Gln Asn Arg Ile Tyr
 260 265 270
 35 Leu Thr Ala Asp Asn Leu Val Leu Asn Leu Gln Asp Glu Ser Phe Thr
 275 280 285
 40 Arg Gly Ser Asp Ser Leu Ile Lys Gly Lys Lys
 290 295

45 (2) INFORMATION FOR SEQ ID NO: 284:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 18 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 284:

Lys Ala Leu Ala Leu Ser Phe His Gly Trp Ser Gly Thr Gly Lys Asn
 1 5 10 15

55 Phe Val

60 (2) INFORMATION FOR SEQ ID NO: 285:

(i) SEQUENCE CHARACTERISTICS:
 (.) LENGTH: 22 amino acids
 (b) TYPE: amino acid
 (D) TOPOLOGY: linear
5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 285:

Asn Leu Ile Asp Tyr Phe Ile Pro Phe Leu Pro Leu Glu Tyr Arg His
 1 5 10 15
10 Val Arg Leu Cys Ala Arg
 20

15 (2) INFORMATION FOR SEQ ID NO: 286:

 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 20 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 286:

Asn Leu Ile Asp Tyr Phe Ile Pro Phe Leu Pro Leu Glu Tyr Arg His
25 1 5 10 15

Val Arg Leu Cys
 20

30 (2) INFORMATION FOR SEQ ID NO: 287:

 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 26 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 287:

40 Cys His Gln Thr Leu Phe Ile Phe Asp Glu Ala Glu Lys Leu His Pro
 1 5 10 15

Gly Leu Leu Glu Val Leu Gly Pro His Leu
 20 25
45 (2) INFORMATION FOR SEQ ID NO: 288:

50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 21 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 288:

Pro Glu Lys Ala Leu Ala Leu Ser Phe His Gly Trp Ser Gly Thr Gly
 1 5 10 15

Lys Asn Phe Val Ala
 20
60

- 5 (2) INFORMATION FOR SEQ ID NO: 289:
- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 23 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 289:
- Asn Leu Lys Glu Lys Ile Phe Ile Ser Phe Ala Trp Leu Pro Lys Ala
1 5 10 15
- 15 Thr Val Gln Ala Ala Ile Gly
20
- 20 (2) INFORMATION FOR SEQ ID NO: 290:
- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 17 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 290:
- Trp Leu Pro Lys Ala Thr Val Gln Ala Ala Ile Gly Ser Val Ala Leu
1 5 10 15
- 30 Asp
- 35 (2) INFORMATION FOR SEQ ID NO: 291:
- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 18 amino acids
- 40 (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 291:
- His Asp Arg Thr Met Gln Asp Ile Val Tyr Lys Leu Val Pro Gly Leu
45 1 5 10 15
- Gln Glu
- 50 (2) INFORMATION FOR SEQ ID NO: 292:
- (i) SEQUENCE CHARACTERISTICS:
- 55 (A) LENGTH: 23 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 292:
- 60 Phe Ala Ser His Asp Arg Thr Met Gln Asp Ile Val Tyr Lys Leu Val

10 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 17 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 293:

20

25

30

35

40 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 295:

50

55 (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 296:

60

Lys Thr Asp Val His Tyr Arg Ser Leu Asp Gly Glu Gly Asn Phe Asn
1 5 10 15

Trp Arg Phe

5

(2) INFORMATION FOR SEQ ID NO: 297:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 297:

Pro Arg Leu Ile Ile Gln Ile Trp Asp Asn Asp Lys Phe Ser Leu Asp
1 5 10 15

20

Asp Tyr Leu Gly Phe Leu Glu Leu Asp Leu
20 25

25

(2) INFORMATION FOR SEQ ID NO: 298:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids

(B) TYPE: amino acid

30

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 298:

Ala Val Met Ile Gly Asp Asp Cys Arg Asp Asp Val Gly Gly Ala
1 5 10 15

35

(2) INFORMATION FOR SEQ ID NO: 299:

40

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 17 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 299:

Ile Leu Val Lys Thr Gly Lys Tyr Arg Ala Ser Asp Glu Glu Lys Ile
1 5 10 15

50

Asn

55

(2) INFORMATION FOR SEQ ID NO: 300:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 277 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 300:

354

Met Asp Ser Met Pro Glu Pro Ala Ser Arg Cys Leu Leu Leu Leu Pro
 1 5 10 15
 5 Leu Leu Leu Leu Leu Leu Leu Leu Leu Pro Ala Pro Glu Leu Gly Pro
 20 25 30
 Ser Gln Ala Gly Ala Glu Glu Asn Asp Trp Val Arg Leu Pro Ser Lys
 35 40 45
 10 Cys Glu Val Cys Lys Tyr Val Ala Val Glu Leu Lys Lys Pro Leu Arg
 50 55 60
 Lys Arg Gln Asp Thr Glu Val Ile Gly Thr Val Tyr Gly Ile Leu Asp
 15 65 70 75 80
 Gln Lys Ala Ser Gly Val Lys Tyr Thr Lys Ser Asp Leu Arg Leu Ile
 85 90 95
 20 Glu Val Thr Glu Thr Ile Cys Lys Arg Leu Leu Asp Tyr Ser Leu His
 100 105 110
 Lys Glu Arg Thr Gly Ser Xaa Arg Phe Ala Lys Gly Met Ser Glu Thr
 115 120 125
 25 Phe Glu Thr Leu His Xaa Leu Val His Lys Gly Val Lys Val Val Met
 130 135 140
 Asp Ile Pro Tyr Glu Leu Trp Asn Glu Thr Ser Ala Glu Val Ala Asp
 145 150 155 160
 Leu Lys Lys Gln Cys Asp Val Leu Val Glu Glu Phe Glu Glu Val Ile
 165 170 175
 35 Glu Asp Trp Tyr Arg Asn His Gln Glu Glu Asp Leu Thr Glu Phe Leu
 180 185 190
 Cys Ala Asn His Val Leu Lys Gly Lys Asp Thr Ser Cys Leu Ala Glu
 195 200 205
 40 Gln Trp Ser Gly Lys Lys Gly Asp Thr Ala Ala Leu Gly Gly Lys Lys
 210 215 220
 Ser Lys Lys Lys Ser Ile Arg Ala Lys Ala Ala Gly Gly Arg Ser Ser
 45 225 230 235 240
 Ser Ser Lys Gln Arg Lys Glu Leu Gly Gly Leu Glu Gly Asp Pro Ser
 245 250 255
 50 Pro Glu Glu Asp Glu Gly Ile Gln Lys Ala Ser Pro Leu Thr His Ser
 260 265 270
 Pro Pro Asp Glu Leu
 275
 55

(2) INFORMATION FOR SEQ ID NO: 301:

60 (i) SEQUENCE CHARACTERISTICS:

355

(A) LENGTH: 199 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 301:

5

Met Asp Gly Gln Lys Lys Asn Trp Lys Asp Lys Val Val Asp Leu Leu
 1 5 10 15

10

Tyr Trp Arg Asp Ile Lys Lys Thr Gly Val Val Phe Gly Ala Ser Leu
 20 25 30

Phe Leu Leu Leu Ser Leu Thr Val Phe Ser Ile Val Ser Val Thr Ala
 35 40 45

15

Tyr Ile Ala Leu Ala Leu Leu Ser Val Thr Ile Ser Phe Arg Ile Tyr
 50 55 60

Lys Gly Val Ile Gln Ala Ile Gln Lys Ser Asp Glu Gly His Pro Phe
 65 70 75 80

20

Arg Ala Tyr Leu Glu Ser Glu Val Ala Ile Ser Glu Glu Leu Val Gln
 85 90 95

25

Lys Tyr Ser Asn Ser Ala Leu Gly His Val Asn Cys Thr Ile Lys Glu
 100 105 110

Leu Arg Arg Leu Phe Leu Val Asp Asp Leu Val Asp Ser Leu Lys Phe
 115 120 125

30

Ala Val Leu Met Trp Val Phe Thr Tyr Val Gly Ala Leu Phe Asn Gly
 130 135 140

Leu Thr Leu Leu Ile Leu Ala Leu Ile Ser Leu Phe Ser Val Pro Val
 145 150 155 160

35

Ile Tyr Glu Arg His Gln Ala Gln Ile Asp His Tyr Leu Gly Leu Ala
 165 170 175

Asn Lys Asn Val Lys Asp Ala Met Ala Lys Ile Gln Ala Lys Ile Pro
 180 185 190

40

Gly Leu Lys Arg Lys Ala Glu
 195

45

(2) INFORMATION FOR SEQ ID NO: 302:

(i) SEQUENCE CHARACTERISTICS:

50

(A) LENGTH: 15 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 302:

55

Met Ala Val Thr Leu Ser Leu Leu Leu Gly Gly Arg Val Cys Ala
 1 5 10 15

60

(2) INFORMATION FOR SEQ ID NO: 303:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 41 amino acids.

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 303:

Pro Ser Leu Ala Val Gly Ser Arg Pro Gly Gly Trp Arg Ala Gln Ala
 1 5 10 15
 Leu Leu Ala Gly Ser Arg Thr Pro Ile Pro Thr Gly Ser Arg Arg Asn
 20 25 30
 Gly Ser Cys Arg Arg Trp Arg Ala Pro
 35 40

(2) INFORMATION FOR SEQ ID NO: 304:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 56 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 304:

Met Ala Val Thr Leu Ser Leu Leu Leu Gly Gly Arg Val Cys Ala Pro
 1 5 10 15
 Ser Leu Ala Val Gly Ser Arg Pro Gly Gly Trp Arg Ala Gln Ala Leu
 20 25 30
 Leu Ala Gly Ser Arg Thr Pro Ile Pro Thr Gly Ser Arg Arg Asn Gly
 35 40 45
 Ser Cys Arg Arg Trp Arg Ala Pro
 50 55

(2) INFORMATION FOR SEQ ID NO: 305:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 481 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 305:

GATGTTACAC AGCTCTTTAA TAATAGTGGC CATAGCTGTA ATAACAATGA CAACAGTAGG 60
 TAACGGTAGT CATACCAACA GTAGGGCAGT GCATTTTATA TTACAACTGG TTTCTTGCTC 120
 TAGTAGGCTT GGGGATGGGT GAAGACGGAC AGGGCTGGCG CAGACCCCTT CCTTCTCCTC 180
 TCCAGCCAC AGTGATCTGG GCTTTTACAA GACAGCCTGC TTCCATTGAG TAGTGTGGGA 240
 AAGTTCCTTC TTGGCTTAGC AATACCCCTG AGACCTTGTT CAGTGGGCTG TGTCTCTCCC 300

TGGGATGCTG GGAGCACCAA GTGTGGCCGA GCTAGGGCTG CTGACTTCCT CTGGGCGCCT 360
CTGGGCTCGG AGGGTCTCTT ATAGGAATTG AGGCCCTTTG CTGCTCCAAG AAATGCTGAG 420
5 GCTGTGGGCA RAGGGKTGTA CCAAGGGGA CTCCTGCTCT GTGTCTGACT TTGGGGATC 480
C 481

10

(2) INFORMATION FOR SEQ ID NO: 306:

(i) SEQUENCE CHARACTERISTICS:
15 (A) LENGTH: 58 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 306:

CACAGCTCTT TAATAATAGT GGCCATAGCT GTAATAACAA TGACAACAGT AGGTAACG 58

25

(2) INFORMATION FOR SEQ ID NO: 307:

(i) SEQUENCE CHARACTERISTICS:
30 (A) LENGTH: 59 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 307:

TGTGTCTCTC CTTGGGATGC TGGGAGCACC AAGTGTGGCC GAGCTAGGGC TGCTGACTT 59

40

(2) INFORMATION FOR SEQ ID NO: 308:

(i) SEQUENCE CHARACTERISTICS:
45 (A) LENGTH: 85 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 308:

GCGAGGGTCT CTTATAGGAA TTGAGGCCCT TTGCTGCTCC AAGAAATGCT GAGGCTGTGG 60

GCGARAGGGKT GTACCCAAGG GGACT 85

55

60 (2) INFORMATION FOR SEQ ID NO: 309:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 34 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 309:

Met Val Gly Pro Val Thr Leu His Lys Lys Ile His Thr Thr Thr Val
 1 5 10 15

10 Leu Phe Ile Val Gln Ile His Ile Leu Leu Ile Gln Ala Ile Thr Gln
 20 25 30

Ala Lys

15

(2) INFORMATION FOR SEQ ID NO: 310:

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 67 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 310:

Leu Gln Met His Leu Met Ile Leu Gln Met Thr Gly Leu Ser Ile Leu
 1 5 10 15

30 Ala Leu Leu Gly Lys Ser Thr Thr Thr Ile Val Glu Gln Lys Phe His
 20 25 30

Asn Gly Lys Asn Gln Lys Ser Gly Leu Lys Glu Asn Arg Asp Lys Lys
 35 40 45

35 Lys Gln Thr Arg Trp Gln Ser Thr Ala Ser Gln Lys Ile Gly Ile Thr
 50 55 60

Glu Glu Arg
 65

40

(2) INFORMATION FOR SEQ ID NO: 311:

45 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 101 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 311:

Met Val Gly Pro Val Thr Leu His Lys Lys Ile His Thr Thr Thr Val
 1 5 10 15

55 Leu Phe Ile Val Gln Ile His Ile Leu Leu Ile Gln Ala Ile Thr Gln
 20 25 30

Ala Lys Leu Gln Met His Leu Met Ile Leu Gln Met Thr Gly Leu Ser
 35 40 45

60 Ile Leu Ala Leu Leu Gly Lys Ser Thr Thr Thr Ile Val Glu Gln Lys

359

50 55 60

Phe His Asn Gly Lys Asn Gln Lys Ser Gly Leu Lys Glu Asn Arg Asp
 65 70 75 80

5 Lys Lys Lys Gln Thr Arg Trp Gln Ser Thr Ala Ser Gln Lys Ile Gly
 85 90 95

10 Ile Thr Glu Glu Arg
 100

15 (2) INFORMATION FOR SEQ ID NO: 312:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 74 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 312:

Met Gln Thr Cys Pro Leu Val Gly Thr Leu Leu Thr Arg Asn Met Asp
 1 5 10 15

25 Gly Tyr Thr Cys Ala Val Val Thr Ser Thr Ser Phe Trp Ile Ile Ser
 20 25 30

Ala Trp Xaa Leu Trp Lys Gly Ser Pro Ser Thr Ser Met Pro Thr Met
 35 40 45

30 Pro Glu Thr Pro Leu Arg Thr Leu Cys Cys Thr Lys Met Pro Ser Ile
 50 55 60

Phe Ser Ser Leu Met Thr Asp Gly Arg Ala
 35 65 70

40 (2) INFORMATION FOR SEQ ID NO: 313:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 78 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 313:

Met Thr Leu Ile Gln Asn Cys Trp Tyr Ser Trp Leu Phe Phe Gly Phe
 1 5 10 15

50 Phe Phe His Phe Leu Arg Lys Ser Ile Ser Ile Phe Ser Ile Phe Leu
 20 25 30

Val Cys Phe Arg Ile Leu Ala Leu Gly Pro Thr Cys Phe Leu Val Trp
 35 40 45

55 Phe Trp Lys Ala Phe Phe Arg His Ile Leu Ile Phe Ile Cys Leu Ser
 50 55 60

Arg Glu Val Phe Arg Pro Arg Cys Phe Leu Val Tyr Phe Arg
 60 65 70 75

(2) INFORMATION FOR SEQ ID NO: 314:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 71 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 314:

Met Gly Thr Arg Ala Gln Val Thr Pro Gly Arg Leu Pro Ile Pro Pro
 1 5 10 15

15

Pro Ala Pro Gly Leu Pro Phe Ser Ala Xaa Glu Pro Leu Gln Gly Gln
 20 25 30

Leu Arg Arg Val Ser Ser Ser Arg Gly Gly Phe Pro Gly Leu Ala Leu
 35 40 45

20

Gln Leu Leu Arg Ser Glu Thr Val Lys Ala Tyr Val Asn Asn Glu Ile
 50 55 60

25

Asn Ile Leu Ala Ser Phe Phe
 65 70

(2) INFORMATION FOR SEQ ID NO: 315:

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 40 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 315:

Met Leu Val Arg Thr Arg Pro Ser Gln Pro Leu Pro Leu Pro Gly Val
 1 5 10 15

40

Gly Leu Gly Gly Pro Arg Ser Gly Asp Pro Pro Glu Ser Thr Glu Leu
 20 25 30

Arg Lys Gly Pro Gly Phe Leu Ala
 35 40

45

(2) INFORMATION FOR SEQ ID NO: 316:

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 262 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 316:

Met Cys Pro Val Cys Gly Arg Ala Leu Ser Ser Pro Gly Ser Leu Gly
 1 5 10 15

60

Arg His Leu Leu Ile His Ser Glu Asp Gln Arg Ser Asn Cys Ala Val
 20 25 30

Cys Gly Ala Arg Phe Thr Ser His Ala Thr Phe Asn Ser Glu Lys Leu
 35 40 45
 5 Pro Glu Val Leu Asn Met Glu Ser Leu Pro Thr Val His Asn Glu Gly
 50 55 60
 Pro Ser Ser Ala Glu Gly Lys Asp Ile Ala Phe Ser Pro Pro Val Tyr
 65 70 75 80
 10 Pro Ala Gly Ile Leu Leu Val Cys Asn Asn Cys Ala Ala Tyr Arg Lys
 85 90 95
 Xaa Leu Glu Ala Gln Thr Pro Ser Val Xaa Lys Trp Ala Leu Arg Arg
 100 105 110
 15 Gln Asn Glu Pro Leu Glu Val Arg Leu Gln Arg Leu Glu Arg Glu Arg
 115 120 125
 Thr Ala Lys Lys Ser Arg Arg Asp Asn Glu Thr Pro Glu Glu Arg Glu
 130 135 140
 Val Arg Arg Met Arg Asp Arg Glu Ala Lys Arg Leu Gln Arg Met Gln
 145 150 155 160
 25 Glu Thr Asp Glu Gln Arg Ala Arg Arg Leu Gln Arg Asp Arg Glu Ala
 165 170 175
 Met Arg Leu Lys Arg Ala Asn Glu Thr Pro Glu Lys Arg Gln Ala Arg
 180 185 190
 30 Leu Ile Arg Glu Arg Glu Ala Lys Arg Leu Lys Arg Arg Leu Glu Lys
 195 200 205
 Met Asp Met Met Leu Arg Ala Gln Phe Gly Gln Asp Pro Ser Ala Met
 210 215 220
 35 Ala Ala Leu Ala Ala Glu Met Asn Phe Phe Gln Leu Pro Val Ser Gly
 225 230 235 240
 40 Val Glu Leu Asp Xaa Gln Leu Leu Gly Lys Met Ala Phe Glu Glu Gln
 245 250 255
 Asn Ser Ser Xaa Leu His
 260
 45

(2) INFORMATION FOR SEQ ID NO: 317:

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 190 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: linear

55

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 317:

Met Asp His Ser His His Met Gly Met Ser Tyr Met Asp Ser Asn Ser
 1 5 10 15

60

Thr Met Gln Pro Ser His His His Pro Thr Thr Ser Ala Ser His Ser

362

20 25 30
 His Gly Gly Gly Asp Ser Ser Met Met Met Met Pro Met Thr Phe Tyr
 35 40 45
 5 Phe Gly Phe Lys Asn Val Glu Leu Leu Phe Ser Gly Leu Val Ile Asn
 50 55 60
 10 Thr Ala Gly Glu Met Ala Gly Ala Phe Val Ala Val Phe Leu Leu Ala
 65 70 75 80
 Met Phe Tyr Glu Gly Leu Lys Ile Ala Arg Glu Ser Leu Leu Arg Lys
 85 90 95
 15 Ser Gln Val Ser Ile Arg Tyr Asn Ser Met Pro Val Pro Gly Pro Asn
 100 105 110
 Gly Thr Ile Leu Met Glu Thr His Lys Thr Val Gly Gln Gln Met Leu
 115 120 125
 20 Ser Phe Pro His Leu Leu Gln Thr Val Leu His Ile Ile Gln Val Val
 130 135 140
 Ile Ser Tyr Phe Leu Met Leu Ile Phe Met Thr Tyr Asn Gly Tyr Leu
 25 145 150 155 160
 Cys Ile Ala Xaa Ala Ala Gly Ala Gly Thr Gly Tyr Phe Leu Phe Ser
 165 170 175
 30 Trp Lys Lys Ala Val Val Val Asp Ile Thr Glu His Cys His
 180 185 190

35 (2) INFORMATION FOR SEQ ID NO: 318:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 123 amino acids

(B) TYPE: amino acid

40 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 318:

Met Val Gln Pro Cys Gly Ala Cys Ala Lys Thr Xaa Trp Lys Ala Cys
 1 5 10 15
 45 Ser Ser Cys Cys Ser Ser Pro Cys Cys Leu Gln Glu Arg Trp Pro Xaa
 20 25 30
 Pro Xaa Ala Xaa Cys Pro Glu Xaa Gly Pro Ser Ser His Pro Gly Ile
 50 35 40 45
 Gln Ala Leu Cys Ala Val Ala Val Val Tyr Leu Ser Pro Ser Ser Arg
 50 55 60
 55 Leu Asp Trp Ser Leu Ala Pro Leu Phe Val Pro Ser Leu Ala Ala Gly
 65 70 75 80
 Glu Thr Pro Leu Thr Gln Pro Ala Trp Ala Leu Thr Thr Asn Thr Leu
 85 90 95
 60

363

Gly His Gly Gln Pro Ala Gln Asp Arg Leu Pro Ala Leu Gly His Cys
 100 105 110

5 Ala Pro Ile Ser Val Leu Gly Leu Gly Ser Ser
 115 120

(PCT Rule 13*bis*)

| | |
|--|--|
| A. The indications made below relate to the microorganism referred to in the description on page <u>75</u> , line <u>N/A</u> | |
| B. IDENTIFICATION OF DEPOSIT | |
| Further deposits are identified on an additional sheet <input type="checkbox"/> | |
| Name of depositary institution <p style="text-align: center;">American Type Culture Collection</p> | |
| Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | |
| Date of deposit April 28, 1997 | Accession Number 209012 |
| C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/> | |
| | |
| D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States) | |
| | |
| E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) | |
| The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposits") | |
| | |
| For receiving Office use only | For International Bureau use only |
| <input checked="" type="checkbox"/> This sheet was received with the international application | <input type="checkbox"/> This sheet was received by the International Bureau on: |
| Authorized officer <p style="text-align: center;">Lydel Meadows Paralegal Specialist IAPD-PCT Operations (703) 305-3745</p> | Authorized officer |

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| | | | |
|--|--------|----------------------------------|------------|
| Applicant's or agent's file reference number | 008PCT | International application number | Unassigned |
|--|--------|----------------------------------|------------|

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

| | |
|---|--|
| A. The indications made below relate to the microorganism referred to in the description on page <u>75</u> , line <u>N/A</u> | |
| B. IDENTIFICATION OF DEPOSIT | |
| Further deposits are identified on an additional sheet <input type="checkbox"/> | |
| Name of depositary institution American Type Culture Collection | |
| Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | |
| Date of deposit June 5, 1997 | Accession Number 209089 |
| C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/> | |
| | |
| D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (If the indications are not for all designated States) | |
| | |
| E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) | |
| The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit") | |
| | |
| For receiving Office use only | For International Bureau use only |
| <input checked="" type="checkbox"/> This sheet was received with the international application | <input type="checkbox"/> This sheet was received by the International Bureau on: |
| Authorized officer Lydell Meadows Paralegal Specialist IAPD-PCT Operations (703) 305-3745 | Authorized officer |

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| | | | |
|---|---------|---------------------------|------------|
| Applicant's or agent's file reference number | 2008PCT | International application | Unassigned |
|---|---------|---------------------------|------------|

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

| | |
|---|--|
| A. The indications made below relate to the microorganism referred to in the description on page 78, line N/A | |
| B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/> | |
| Name of depositary institution American Type Culture Collection | |
| Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | |
| Date of deposit June 5, 1997 | Accession Number 209090 |
| C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/> | |
| | |
| D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (If the indications are not for all designated States) | |
| | |
| E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) | |
| The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit") | |
| For receiving Office use only | |
| <input checked="" type="checkbox"/> This sheet was received with the international application | <input type="checkbox"/> This sheet was received by the International Bureau on: |
| Authorized officer Lydell Meadows Paralegal Specialist IAPD-PCT Operations (703) 305-3745 | Authorized officer |

| | | | | |
|--|--------|-----|-----------------------------|------------|
| Applicant's or agent's file reference number | 008PCT | 367 | International application ? | Unassigned |
|--|--------|-----|-----------------------------|------------|

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

| | |
|---|--|
| A. The indications made below relate to the microorganism referred to in the description on page 80, line N/A | |
| B. IDENTIFICATION OF DEPOSIT | |
| Further deposits are identified on an additional sheet <input type="checkbox"/> | |
| Name of depositary institution American Type Culture Collection | |
| Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | |
| Date of deposit May 22, 1997 | Accession Number 209076 |
| C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/> | |
| | |
| D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (If the indications are not for all designated States) | |
| | |
| E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) | |
| The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit") | |
| | |
| For receiving Office use only | |
| <input checked="" type="checkbox"/> This sheet was received with the international application | |
| Authorized officer | Lydet Meadows Paralegal Specialist IAPD-PCT Operations (703) 305-3745 |
| For International Bureau use only | |
| <input type="checkbox"/> This sheet was received by the International Bureau on: | |
| Authorized officer | |

| | | | |
|--|--------|---------------------------|------------|
| Applicant's or agent's file reference number | 008PCT | International application | Unassigned |
|--|--------|---------------------------|------------|

(PCT Rule 13bis)

| | |
|--|---|
| A. The indications made below relate to the microorganism referred to in the description on page <u>82</u> , line <u>N/A</u> | |
| B. IDENTIFICATION OF DEPOSIT <div style="text-align: right;">Further deposits are identified on an additional sheet <input type="checkbox"/></div> | |
| Name of depositary institution <div style="text-align: center;">American Type Culture Collection</div> | |
| Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | |
| Date of deposit May 29, 1997 | Accession Number 209086 |
| C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/> | |
| | |
| D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States) | |
| | |
| E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) | |
| The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit") | |
| | |
| For receiving Office use only <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> <input checked="" type="checkbox"/> This sheet was received with the international application </div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> Authorized officer: Lydell Meadows Paralegal Specialist APD-PCT Operations (703) 305-3745 </div> | For International Bureau use only <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> <input type="checkbox"/> This sheet was received by the International Bureau on: </div> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> Authorized officer: </div> |

369

| | | | |
|--|--------|-----------------------------|------------|
| Applicant's or agent's file reference number | 008PCT | International application ? | Unassigned |
|--|--------|-----------------------------|------------|

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13bis)

| | |
|---|-------------------------|
| A. The indications made below relate to the microorganism referred to in the description on page 83, line N/A | |
| B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet <input type="checkbox"/> | |
| Name of depositary institution American Type Culture Collection | |
| Address of depositary institution (including postal code and country) 10801 University Boulevard Manassas, Virginia 20110-2209 United States of America | |
| Date of deposit June 19, 1997 | Accession Number 209126 |
| C. ADDITIONAL INDICATIONS (leave blank if not applicable) This information is continued on an additional sheet <input type="checkbox"/> | |
| | |
| D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE (if the indications are not for all designated States) | |
| | |
| E. SEPARATE FURNISHING OF INDICATIONS (leave blank if not applicable) | |
| The indications listed below will be submitted to the International Bureau later (specify the general nature of the indications, e.g., "Accession Number of Deposit") | |
| <div style="display: flex; justify-content: space-between;"><div style="width: 45%;">For receiving Office use only <input checked="" type="checkbox"/> This sheet was received with the international application Authorized officer Lydell Meadows Paralegal Specialist IAPD-PCT Operations (703) 305-3745</div><div style="width: 45%;">For International Bureau use only <input type="checkbox"/> This sheet was received by the International Bureau on: Authorized officer</div></div> | |

What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
 - (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
 - (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
 - (c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
 - (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;
 - (e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X, having biological activity;
 - (f) a polynucleotide which is a variant of SEQ ID NO:X;
 - (g) a polynucleotide which is an allelic variant of SEQ ID NO:X;
 - (h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
 - (i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.
3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.
5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.
7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.
8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.
9. A recombinant host cell produced by the method of claim 8.
10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:
- (a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z, having biological activity;
 - (c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (e) a secreted form of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;
 - (f) a full length protein of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

- (g) a variant of SEQ ID NO:Y;
- (h) an allelic variant of SEQ ID NO:Y; or
- (i) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the secreted form or the
5 full length protein comprises sequential amino acid deletions from either the C-terminus
or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of
claim 11.

10

14. A recombinant host cell that expresses the isolated polypeptide of claim
11.

15. A method of making an isolated polypeptide comprising:
15 (a) culturing the recombinant host cell of claim 14 under conditions such that
said polypeptide is expressed; and
(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

20

17. A method for preventing, treating, or ameliorating a medical condition,
comprising administering to a mammalian subject a therapeutically effective amount of
the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a
25 pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of
claim 1; and
(b) diagnosing a pathological condition or a susceptibility to a pathological
30 condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a
pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of
35 claim 11 in a biological sample; and
(b) diagnosing a pathological condition or a susceptibility to a pathological
condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:
- 5 (a) contacting the polypeptide of claim 11 with a binding partner; and
(b) determining whether the binding partner effects an activity of the polypeptide.
21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
- 10 22. A method of identifying an activity in a biological assay, wherein the method comprises:
- 15 (a) expressing SEQ ID NO:X in a cell;
(b) isolating the supernatant;
(c) detecting an activity in a biological assay; and
(d) identifying the protein in the supernatant having the activity.
23. The product produced by the method of claim 22.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/12125

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.
US CL : 435/69.1, 70.1, 71.1, 235.1, 243, 325, 410; 536/23.1, 23.5

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/69.1, 70.1, 71.1, 235.1, 243, 325, 410; 536/23.1, 23.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| Y | EP 0 679 016 A1 (MATSUBARA et al.) 11 February 1995, see entire document and sequence listing, especially SEQ ID NO. 12, position 585-605 versus reference sequence at position 42-62; SEQ ID NO. 13, position 1942-5189 versus reference sequence at position 1-248; SEQ ID NO. 15, position 569-817 versus reference sequence at position 1-249; SEQ ID NO. 16, position 233-586 versus reference sequence at position 1-354; and SEQ ID NO. 18, position 1309-1699 versus reference sequence at position 12-393. | 1-10, 14, 15, and 21 |
| Y | WO 96/40917 A1 (YALE UNIVERSITY.) 19 December 1996. See entire document and sequence listing, especially SEQ ID NO. 11, position 444-692 versus reference sequence at position 2-250. | 1-10, 14, 15, and 21 |

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

| | |
|--|---|
| * Special categories of cited documents: | * later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| *A* document defining the general state of the art which is not considered to be of particular relevance | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| *B* earlier document published on or after the international filing date | *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *A* document member of the same patent family |
| *O* document referring to an oral disclosure, use, exhibition or other means | |
| *P* document published prior to the international filing date but later than the priority date claimed | |

Date of the actual completion of the international search
08 SEPTEMBER 1998

Date of mailing of the international search report
01 OCT 1998

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Authorized officer
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Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/12125

| C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|---|---|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| Y | WO 95/27791 A1 (DAVIES et al.) 19 October 1995, See entire document and sequence listing, especially SEQ ID NO. 17, position 742-799 versus reference sequence at position 1334-1391. | 1-10, 14, 15, and 21 |
| Y | WO 95/14100 A1 (THE WELLCOME FOUNDATION LIMITED) 26 May 1995. See entire document and sequence listing, especially SEQ ID NO. 97, position 966-991 versus reference sequence at position 747-772. | 1-10, 14, 15, 21 |
| Y | WO 94/28133 A1 (AMGEN INC.) 08 December 1994, see entire document and sequence listing, especially SEQ ID NO. 14, position 758-808 versus reference sequence at position 1599-1649. | 1-10, 14, 15, and 21 |
| Y | WO 95/01437 A2 (REGENTS OF THE UNIVERSITY OF MINNESOTA) 12 January 1995, see entire document and sequence listing, especially SEQ ID NO. 19, position 69-122 versus reference sequence at position 604-657. | 1-10, 14, 15, and 21 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/12125

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-10, 14 15 and 21

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/12125

A. CLASSIFICATION OF SUBJECT MATTER: IPC (6):

C07H 21/02, 04; C12N 5/00, 5/04, 5/06, 5/10, 5/16; 15/00, 15/09, 15/10, 15/11, 15/12; C12P 21/04, 21/06

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

Databases: Genbank, embase, biosis, medline

Search Terms/Strategy: Sequence search of Sequences 11-19 and 97; est; secret?; moore?/au; shi?/au; rosen?/au; ruben?/au; lafleu?/au; olsen?/au; ebner?/au; brewer?/au; young?/au; greene?/au; ferrie?/au; yu ?/au; ni ?/au; feng ?/au

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I:

Claims 1-10, 14, 15, and 21 drawn to a polynucleotide(s), vector(s) containing the polynucleotide, host cells containing the vector(s) which are SEQ ID NO: X or a polynucleotide encoding the polypeptide Y or a cDNA in the material deposited with American Type Culture Collection with accession number Z wherein the cDNA in Z hybridizes to X. Additionally Group I contains the first method making the cells (claim 14) containing the vector(s) containing the polynucleotide(s) and the first method of use of the cells (claim 15) to make a product. There appear to be a total of 46 polynucleotide sequences of which the first ten (10) are selected for examination and therefore, there are nine (9) remaining additional groups of four (4) polynucleotide sequences.

Group II:

Claims 11, 12, 16, and 23 drawn to polypeptides and/or fragments thereof with the amino acid sequence defined by SEQ ID NO: Y as found in the material deposited with the American Type Culture Collection with accession number Z. There appear to be a total of 74 polypeptide sequences and therefore 73 additional species of proteins.

Group III:

Claim 13, drawn to an antibody that binds to a polypeptide with the amino acid sequence defined by SEQ ID NO: Y as found in the material deposited with the American Type Culture Collection with accession number Z. There appear to be a total of 74 antibodies that correspond to the SEQ ID NOs: for the "Y" and "Z" sequences and therefore 73 additional species of proteins.

Group IV:

Claim 17, drawn to a process of preventing, treating, or ameliorating a medical condition by administering a polypeptide or a polynucleotide which a second/alternative process of use of the second product and of an alternative process of use of the first claimed product in Group I.

In Group IV, and where additional fees are paid, the claims are searched only insofar as they are applicable to the selected polypeptide and its corresponding SEQ ID NO: as the first species as directed to a process practiced using a polypeptide. The second species is the practice of the process using a polynucleotide. In each instance, the same selected polypeptide as for the first species of Group II and for the first 10 polynucleotide sequences for Group I would be examined. Applicant may elect to pay additional fees for each additional one of the 73 different polypeptide species beyond the first one (1) polypeptide and/or the first 10 polynucleotides as set forth in the above paragraphs directed to Group I and II.

Group V:

Claim 18, drawn to a method of diagnosis of a pathological condition and another alternative process of use of the first claimed product in Group I. Additionally Group V contains indications that there are a total of 46 polynucleotide sequences and therefore, nine (9) additional groups of four (4) polynucleotide sequences beyond the first ten (10) sequences.

Group VI:

Claim 19, drawn to a method of diagnosis of a pathological condition and another alternative process of use of the polypeptide. There appear to be a total of 74 polypeptide sequences and therefore 73 additional species of proteins.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/12125

Group VII:

Claim 20, drawn to a method of identification of a binding partner for a polypeptide. There appear to be a total of 74 polypeptide sequences and therefore 73 additional species of proteins.

Group VIII:

Claim 22, drawn to a method of identification of function of a protein is another alternative process of use of the product in Group I. Additionally Group V contains indicia that there are a total of 46 polynucleotide sequences and therefore, nine(9) additional groups of four (4) polynucleotide sequences beyond the first ten (10) sequences.

The inventions listed as Groups I through VIII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

Claims of Group I are drawn to nucleotides, nucleotide constructs, and/or methods requiring the use of nucleotides or nucleotide constructs that contain more than ten individual, independent, and distinct nucleotide sequences in alternative form. Accordingly, these claims are subject to lack of unity as outlined in 1192 O.G. 68 (19 November 1996).

For Group I, the first ten (10) of the individual polynucleotide sequences designated as "X" by SEQ ID NO: as set forth in the application (see for example page 29+ and/or the SEQUENCE LISTING) are included for search. The corresponding SEQ ID NO: for "Y" and "Z" for each selected "X" should also be noted. The search of the no more than ten sequences may include the complements of the selected sequences and, where appropriate, may include subsequences within the selected sequences (e.g., oligomeric probes and/or primers).

In Group IV (as directed to the species which are polynucleotides) should applicant pay the additional fee for the second appearing species in Group IV which are polynucleotides, first ten (10) of the individual polynucleotide sequences designated as "X" by SEQ ID NO: as set forth in the application (see for example page 29+ and/or the SEQUENCE LISTING) are included for search of Group IV should the fees for Group IV be paid. This is also applied to Groups V and VIII. The corresponding SEQ ID NO: for "Y" and "Z" for each selected "X" should also be noted. The search of the no more than ten sequences may include the complements of the selected sequences and, where appropriate, may include subsequences within the selected sequences (e.g., oligomeric probes and/or primers).

Where Applicant may elect to pay additional fees for a search of sequences beyond the initial ten (10) polynucleotide sequences, and in accordance with 1192 O.G. 68 (19 November 1996), applicant may select additional groups of polynucleotides consisting of four (4) sequences beyond the initial ten (10) sequences for Group I which would then be searched with Group I upon payment of the requisite fees for the requisite Groups beyond Group I.

As to the polypeptides of Groups II, III, IV (as directed to a species which is a polypeptide), VI, and VII each is a distinct and different protein. Should additional fees for the above indicated Groups be paid, the first amino acid sequence identified from the SEQUENCE LISTING by applicant would be searched with the additional group for which the additional search fees were paid.

Applicant may select additional proteins and or antibodies to be searched by specifying the appropriate SEQ ID NOs and payment of the requisite additional fees for each single additional particular species that are selected beyond the one (1) protein identified by SEQ ID NO:.

The SEQ ID NOs in Group I define, absent evidence to the contrary, structurally distinct and different proteins. Note the present application written description (page 5+) refers to the protein encoded by gene 1 as likely to be involved in promotion of a variety of cancers whereas gene 2 (pages 6-7) is directed to apparently a variety but not correlated immune system disorder(s) whereas gene 3 (pages 7-8) is asserted at page 7 to be a mediator of ligand dependent AF-2. Each of which and absent factual evidence to the contrary, are directed to genes encoding distinct and different proteins and are therefore distinct and different genes and appear to map to different chromosomes.

As to the protein of Group II and the antibody of Group III, each is distinct and different for the reasons indicated in the preceding paragraph and because the proteins have distinct and different chemical, physical, and biological properties from that of DNA/polynucleotides/vectors and cells containing same.

Groups IV through VIII are directed to alternative processes of use of the Group I and II compositions where